GeneDose Genetic Response Report

SAMPLE

NOVALAB Reference Medical Lab

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This report combines (i) an analysis of the patient's DNA, 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 guidance 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: DOE, JANE
Date of Birth: Dec 25, 1950
Gender: Female

Physician: PHYSICIAN
Practice: DOCTORS OFFICE

Date Collected: Feb 2, 2020
Date Accessioned: Feb 6, 2020
Specimen type: Buccal Swab
Sample ID: 20P00000

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Genetic Summary Information

† When multiple activities are listed, check information in Medication Report Details (Pg. 13) for specific medication of interest.
Uncertain = No known diplotype/result (name) or activity for this combination of genetic variants; Uninterpretable Genotype.

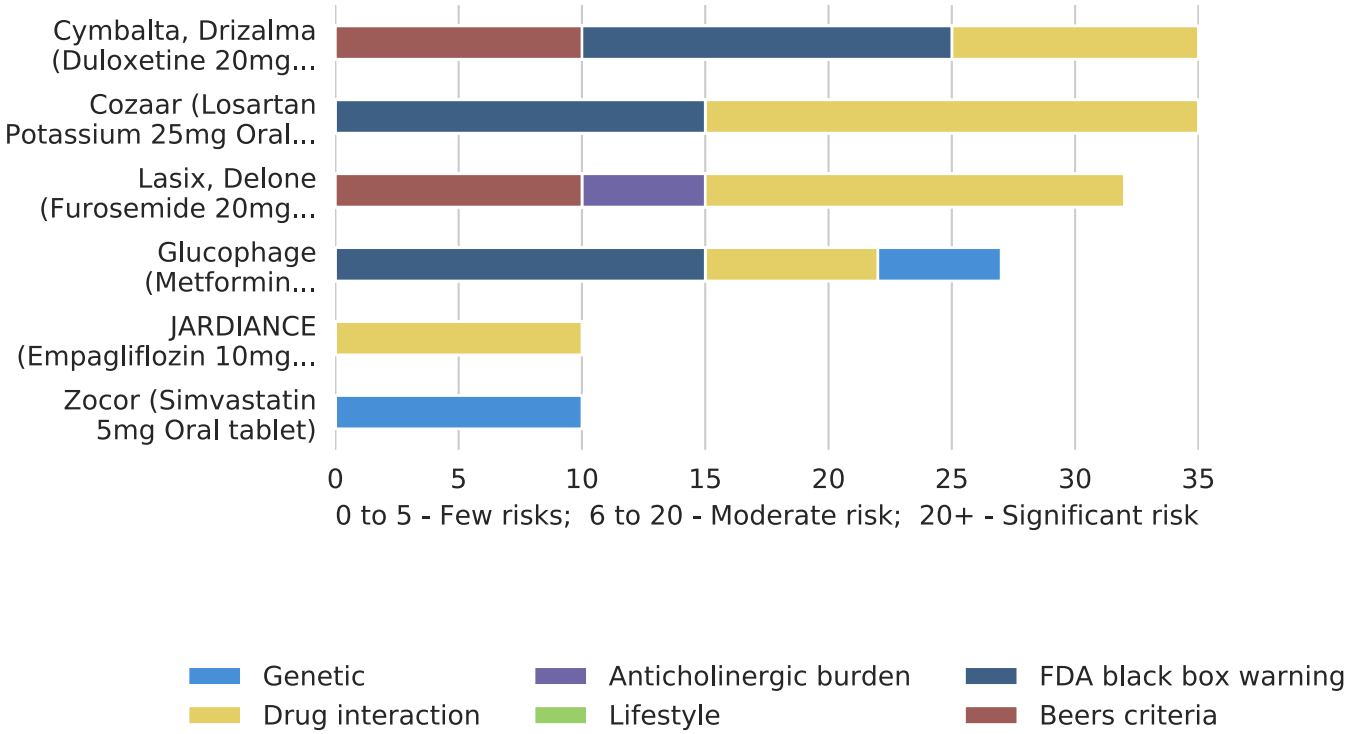
Genetic Summary

Gene	Result	Activity †
ApoE	ε3|ε4	See ApoE Genotype Info.
ATM	A|C	Increased likelihood of treatment success when taking metformin
COMT(Val158Met)	G|G	Multiple statuses; see per-drug detail
CYP1A2	*1F|*1F	Ultrarapid metabolizer
CYP2B6	*1A|*1A	Extensive metabolizer
CYP2C19	*1|*2	Intermediate metabolizer
CYP2C9	*1|*1	Extensive metabolizer
CYP2D6	*2B|*4A or *4K|*39; or *2A|*4A	Intermediate metabolizer
CYP3A4	*1A|*1A	Multiple statuses; see per-drug

Gene	Result	Activity †
		detail
CYP3A5	*3A|*3A; or *3C|*3C; or *3A|*3C	Poor metabolizer
DPYD	*1|*1	Normal function
Factor V Leiden	Normal	See Thrombosis Profile
MTHFR	GT|AT	Reduced function
MTHFR (A1298C)	Normal	See Thrombosis Profile
MTHFR (C677T)	Heterozygous	See Thrombosis Profile
Prothrombin (F2)	Normal	See Thrombosis Profile
SLCO1B1	*1|*5	Intermediate liver uptake activity
VKORC1	*1|*2	Reduced (with respect to Warfarin)

Current Regimen Risk Chart

This chart summarizes the various risk factors associated with each medication entered into GeneDose™ Live for JANE DOE. The length of each colored segment represents the relative contribution of a risk category (detailed in the below legend) to the overall risk associated with the use of a medication. For further information, consult the *Current Regimen Risk Details* Pg. 4 section.



Current Regimen Risk Detail

Severe Risks

American Geriatric Society guidelines

The following products appear on the American Geriatric Society's Beers Criteria for Potentially Inappropriate Medication Use in Older Adults:

- Duloxetine 20mg Oral capsule, gastro-resistant pellets
- Furosemide 20mg Oral tablet

Black box warning for Cozaar (Losartan Potassium 25mg Oral tablet) and teratogenesis

Black box warning for Cymbalta, Drizalma (Duloxetine 20mg Oral capsule, gastro-resistant pellets) and suicidal ideation

Black box warning for Glucophage (Metformin Hydrochloride 500mg Oral tablet) and lactic acidosis

Major Risks

Genetic warning for Zocor (Simvastatin 5mg Oral tablet)

Individuals with intermediate SLCO1B1 liver uptake activity have a moderately increased risk of myopathy when taking a 40 mg/day or higher dose of simvastatin. A reduced dosage or alternate statin drug should be considered.

Moderate Risks

Genetic warning for Glucophage (Metformin Hydrochloride 500mg Oral tablet)

Increased drug efficacy likely.

JARDIANCE (Empagliflozin 10mg Oral tablet) may cause synergistic or additive toxicity with Cozaar (Losartan Potassium 25mg Oral tablet)

- monitor renal function
- monitor blood pressure
- monitor serum potassium

- monitor blood glucose concentration and for changes in glycemic control

Coadministration may result in an increased risk for symptomatic hypotension. Also monitor for changes in volume status, potassium levels, renal function, blood glucose, and glycemic control.

JARDIANCE (Empagliflozin 10mg Oral tablet) effectiveness may be reduced due to aggravation of underlying condition by Lasix, Delone (Furosemide 20mg Oral tablet)

- use combination with caution
- monitor blood glucose concentration and for changes in glycemic control

When empagliflozin is initiated in patients already receiving loop diuretics, volume depletion can occur. Loop diuretics can also decrease the hypoglycemic effects of antidiabetic agents by producing an increase in blood glucose concentrations.

Lasix, Delone (Furosemide 20mg Oral tablet) may cause synergistic or additive toxicity with Cymbalta, Drizalma (Duloxetine 20mg Oral capsule, gastro-resistant pellets)

- monitor for signs of drug toxicity
- monitor serum sodium

Patients receiving a diuretic during treatment with a Serotonin norepinephrine reuptake inhibitor (SNRI) may be at greater risk of developing hyponatremia and/or the syndrome of inappropriate antidiuretic hormone secretion (SIADH).

Glucophage (Metformin Hydrochloride 500mg Oral tablet) has an additive effect with Cozaar (Losartan Potassium 25mg Oral tablet)

- monitor renal function
- monitor blood glucose concentration and for changes in glycemic control

Angiotensin II receptor antagonists (ARBs) may enhance the hypoglycemic effects of metformin by improving insulin sensitivity. Monitored for changes in renal function and glycemic control.

Cymbalta, Drizalma (Duloxetine 20mg Oral capsule, gastro-resistant pellets) has an additive effect with Cozaar (Losartan Potassium 25mg Oral tablet)

- use combination with caution
- monitor blood pressure

Orthostatic hypotension and syncope have been reported during duloxetine administration. The concurrent administration of antihypertensive agents and duloxetine may increase the risk of hypotension. Monitor blood pressure if the combination is necessary.

Lasix, Delone (Furosemide 20mg Oral tablet) may have an additive effect with Cozaar (Losartan Potassium 25mg Oral tablet)

- use combination with caution
- monitor blood pressure

Coadministration of loop diuretics and angiotensin II receptor antagonists may result in severe hypotension and deterioration in renal function, including renal failure.

Minor Risks

Lasix, Delone (Furosemide 20mg Oral tablet) may aggravate underlying condition, thus reducing effectiveness of Glucophage (Metformin Hydrochloride 500mg Oral tablet)

- monitor blood glucose concentration and for changes in glycemic control

Furosemide may cause hyperglycemia and glycosuria in patients with diabetes mellitus, probably due to diuretic-induced hypokalemia.

Thrombosis Profile

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

General Description

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

Patients who are homozygous for MTHFR 677T or MTHFR 1298C may have a further increased risk for venous thrombosis if they also possess the Factor V Leiden 1691A allele. However the MTHFR alleles alone do not predict a significant risk for venous thrombosis.

References and Useful Information:

- Factor V Leiden Working Group; ACMG Laboratory Quality Assurance Molecular Subcommittee of the ACMG Laboratory Quality Assurance Committee AMERICAN COLLEGE OF MEDICAL GENETICS; Standards and Guidelines for Clinical Genetics Laboratories; 2006 Edition
  - Middeldorp S, Henkens CM, Koopman MM, van Pampus ECM,Hamulyák K, van der Meer J, Prins MH, Büller HR. The incidence of venous thromboembolism in family members of patients with factor V Leiden mutation and venous thrombosis. Ann Intern Med 1998;128:15-20.
  - Vandenbroucke JP, Koster T, Briet E, Reitsma PH, Bertina RM, Rosendaal FR. Increased risk of venous thrombosis in oral contraceptive users who are carriers of factor V Leiden mutation. Lancet 1994;344:1453-1457.
  - Rosendaal FR, Koster T, Vandenbroucke JP, Reitsma PH. High risk of thrombosis in patients homozygous for factor V Leiden (activated protein C resistance). Blood 1995;85(6):1504-1508.
  - Reich LM, Bower M, Key NS. Role of the geneticist in testing and counseling for inherited thrombophilia. Genet Med 2003;5:133-143.
  - Tosetto A, Rodeghiero F, Martinelli I, De Stefano V, Missiaglia E, Chiusolo P, Mannucci PM. Additional genetic risk factors for venous thromboembolism in carriers of the factor V Leiden mutation. Br J Haematol 1998;103:871-876.
  - De Stefano V, Martinelli I, Mannucci PM, Paciaroni K, Chiusolo P, Casorelli I, Rossi E, Leone G. The risk of recurrent deep venous thrombosis among heterozygous carriers of both factor V Leiden and the G20210A prothrombin mutation. N Engl J Med 1999;341:801-806.
- M. Adams, P.D. Smith, D. Martin, J.R. Thompson, D. Lodwick, N.J. Samani. Genetic analysis of thermolabile methylenetetrahydrofolate reductase as a risk factor for myocardial infarction. QJM. 1996 Jun;89(6):437-44.

ApoE Genotype Information†

Tested Genes (Alleles)	Genotype	Predicted Phenotype	Clinical Guidance
ApoE (ε2, ε3, ε4)	ε3|ε4	ε4 is often associated with a potential change in LDL cholesterol and plasma triglyceride levels.	There is a potential increased risk of cardiovascular disease and atherosclerosis.

General Description

Genetic analysis in the ApoE gene was performed using molecular genetic techniques. The genotype is based on genotyping results for this patient at SNPs rs429358 and rs7412.

ApoE ε3 is the most common allele—found in about 60% of people. The presence of ε2 or ε4 alleles may be a risk factor for multiple conditions including cardiovascular disease. ApoE ε2 carriers may be more likely to develop familial dysbetalipoproteinemia or type III hyperlipoproteinemia.

† Predicted phenotype, clinical significance, relative risk, and interpretations reported for each genotype are associated with cardiovascular risk only. The interpretations should not be used to determine the relative risk of other diseases. Other factors important to understanding total risk should be considered.

Medication Summary

Cardiac

Therapeutic Class	Standard Precautions	Caution / Info	Change recommended
Antiarrhythmics		Flecainide Propafenone	
Anticoagulants	Acenocoumarol	Warfarin	
Anticonvulsants	Phenytoin		
Antiplatelet Agents	Prasugrel Ticagrelor		Clopidogrel
Beta Blockers	Carvedilol Nebivolol Propranolol	Metoprolol	
Statins	Atorvastatin	Simvastatin	

Gastroenterology

Therapeutic Class	Standard Precautions	Caution / Info	Change recommended
Antidepressants	Mirtazapine Trazodone	Amitriptyline Clomipramine Desipramine Doxepin Nortriptyline	
Antiemetics	Ondansetron	Tropisetron	
Endocrine-Metabolic Agents		Eliglustat	
Immunosuppressants	Cyclosporine		
Nonsteroidal Anti-Inflamatory Drugs (NSAIDs)	Celecoxib		
Proton Pump Inhibitors (PPIs)		Dexlansoprazole Esomeprazole Lansoprazole Omeprazole Pantoprazole Rabeprazole	
Selective Serotonin Reuptake Inhibitors (SSRIs)		Citalopram Escitalopram Paroxetine	

Infectious Disease

Therapeutic Class	Standard Precautions	Caution / Info	Change recommended
Antifungals	Ketoconazole	Voriconazole	

Pain

Therapeutic Class	Standard Precautions	Caution / Info	Change recommended
Analgesics, Opioid	Methadone (CYP2B6)		
Anticonvulsants	Phenytoin	Brivaracetam Clobazam	
Antidepressants	Duloxetine Mirtazapine Moclobemide Trazodone	Amitriptyline Clomipramine Desipramine Doxepin Nortriptyline	

Pain

Therapeutic Class	Standard Precautions	Caution / Info	Change recommended
		Protriptyline Venlafaxine Vortioxetine	
Antipsychotics	Olanzapine		
Beta Blockers	Nebivolol Propranolol		
Endocrine-Metabolic Agents		Eliglustat	
Immunosuppressants	Cyclosporine	Tacrolimus	
Muscle Relaxants			Carisoprodol
Nonsteroidal Anti-Inflamatory Drugs (NSAIDs)	Celecoxib Diclofenac Flurbiprofen Ibuprofen Lornoxicam Meloxicam Piroxicam		
Opioids	Buprenorphine Fentanyl Hydrocodone	Codeine Oxycodone Oxycodone (CYP3A5)	Tramadol
Selective Serotonin Reuptake Inhibitors (SSRIs)	Fluoxetine	Citalopram Escitalopram Fluvoxamine Paroxetine Sertraline	

Psychotropic

Therapeutic Class	Standard Precautions	Caution / Info	Change recommended
Anti-ADHD Agents	Amphetamine Atomoxetine Dexmethylphenidate Dextroamphetamine Guanfacine Lisdexamfetamine Methylphenidate (COMT)		
Anticonvulsants	Phenytoin	Brivaracetam Clobazam	
Antidementia		Donepezil	

Psychotropic

Therapeutic Class	Standard Precautions	Caution / Info	Change recommended
Agents			
Antidepressants	Duloxetine Mirtazapine Moclobemide Trazodone	Amitriptyline Clomipramine Desipramine Doxepin Nortriptyline Protriptyline Venlafaxine Vortioxetine	
Antipsychotics	Brexpiprazole Clozapine Flupenthixol Haloperidol Olanzapine Quetiapine	Aripiprazole Iloperidone Perphenazine Pimozide Risperidone Zuclopenthixol	Thioridazine
Anxiolytics	Alprazolam Buspirone Clonazepam	Diazepam	
Beta Blockers	Propranolol		
Central Monoamine-Depleting Agents		Tetrabenazine	
Central Nervous System Agents		Dextromethorphan-Quinidine	
Cholinesterase Inhibitors	Galantamine		
Hypnotics	Eszopiclone		
Selective Serotonin Reuptake Inhibitors (SSRIs)	Fluoxetine	Citalopram Escitalopram Fluvoxamine Paroxetine Sertraline	

Surgery

Therapeutic Class	Standard Precautions	Caution / Info	Change recommended
Anticholinergic Agents		Tolterodine	
Antiemetics	Ondansetron	Tropisetron	

Surgery

Therapeutic Class	Standard Precautions	Caution / Info	Change recommended
Opioids	Fentanyl		

Other Drugs

Therapeutic Class	Standard Precautions	Caution / Info	Change recommended
Alpha-1 Blockers	Tamsulosin		
Anticholinergic Agents	Fesoterodine		
Antidiabetics	Gliclazide Glimepiride Glyburide Saxagliptin Tolbutamide	Metformin	
Antineoplastic Agents			Methotrexate
Anti-Retroviral Agents	Efavirenz Nevirapine		
Beta-3 Adrenergic Agonists	Mirabegron		
Cholinergic Agonists		Cevimeline	
Contraceptives	Estrogen-containing oral contraceptives		
EGFR Inhibitors	Gefitinib		
Immunosuppressants	Sirolimus		
Vesicular monoamine transporter 2 inhibitor		Deutetrabenazine	

Legend

- Typical response is expected
- Change recommended
- Consider alternative therapy
- 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) *FDA drug label: Actionable PGx*	CYP2D6: Intermediate metabolizer. One allele showing normal function and one showing little or no function.	Typical response is expected; no additional therapeutic recommendations.		
Analgesics, Opioid				
Methadone (CYP2B6) (Dolophine) *FDA drug label: Not established for PGx*	CYP2B6: Extensive metabolizer. Two alleles showing normal activity.	Typical response is expected; no additional therapeutic recommendations.		

Drug		Finding	Recommendation	Concern	Evidence
Anti-ADHD Agents					
Amphetamine (Adzenys, Evekeo) *FDA drug label: Not established for PGx*	✓	COMT(Val158Met): Increased function. Two alleles with increased activity.	Typical response is expected; no additional therapeutic recommendations.		●
Atomoxetine (Strattera) *FDA drug label: Actionable PGx*	✓	CYP2D6: Intermediate metabolizer. One allele showing normal function and one showing little or no function.	Typical response is expected; no additional therapeutic recommendations.		◗
Dexmethylphenidate (Focalin) *FDA drug label: Not established for PGx*	✓	COMT(Val158Met): Increased function. Two alleles with increased activity.	Typical response is expected; no additional therapeutic recommendations.		●
Dextroamphetamine (Zenzedi, Dexedrine) *FDA drug label: Not established for PGx*	✓	COMT(Val158Met): Increased function. Two alleles with increased activity.	Typical response is expected; no additional therapeutic recommendations.		●
Guanfacine (Tenex, Intuniv) *FDA drug label: Not established for PGx*	✓	CYP3A4: Extensive metabolizer. Two alleles showing normal function.	Typical response is expected; no additional therapeutic recommendations.		●
Lisdexamfetamine (Vyvanse) *FDA drug label: Not established for PGx*	✓	COMT(Val158Met): Increased function. Two alleles with increased activity.	Typical response is expected; no additional therapeutic recommendations.		●
Methylphenidate (COMT) (Concerta, Metadate, Ritalin, Ritalin LA, Quillivant, Daytrana, Methylin) *FDA drug label: Not established for PGx*	✓	COMT(Val158Met): Increased function. Two alleles with increased activity.	Typical response is expected; no additional therapeutic recommendations.		●

Drug	Finding	Recommendation	Concern	Evidence
Antiarrhythmics				
Flecainide (Tambocor) *FDA drug label: Not established for PGx*	CYP2D6: Intermediate metabolizer. One allele showing normal function and one showing little or no function.	Individuals with intermediate metabolizer status have the potential for decreased elimination. Consider reducing dose by 25%; record ECG; monitor plasma concentration.	ADR	
Propafenone (Rythmol) *FDA drug label: Actionable PGx*	CYP2D6: Intermediate metabolizer. One allele showing normal function and one showing little or no function.	Individuals with intermediate metabolizer status have decreased metabolism to less active compounds; the resultant increased plasma concentrations may increase the risk proarrhythmia, exaggerated beta-adrenergic blocking activity, and other adverse events. Adjust dose in response to plasma concentration and record ECG or select alternative drug (e.g. sotalol, disopyramide, quinidine, amiodarone).	ADR	
Anticholinergic Agents				
Fesoterodine (Toviaz) *FDA drug label: Actionable PGx*	CYP2D6: Intermediate metabolizer. One allele showing normal function and one showing little or no function.	Typical response is expected; no additional therapeutic recommendations.		
Tolterodine (Detrol) *FDA drug label: Actionable PGx*	CYP2D6: Intermediate metabolizer. One allele showing normal function and one showing little or no function.	Individuals with intermediate metabolizer status may be at an increased risk of adverse drug reactions due to reduced metabolic clearance. Insufficient evidence to allow calculation of dose adjustment. Be alert to adverse reactions including QT prolongation.	ADR	

Drug	Finding	Recommendation	Concern	Evidence
Anticoagulants				
Acenocoumarol (Sintrom, Acitrom) *FDA drug label: Not established for PGx*	CYP2C9: Extensive metabolizer. Two alleles showing normal activity.	Typical response is expected; no additional therapeutic recommendations.		
Warfarin (Coumadin) *FDA drug label: Actionable PGx*	Multigenic: VKORC1, CYP2C9: Extensive metabolizer. Two alleles showing normal activity.	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.		
Anticonvulsants				
Brivaracetam *FDA drug label: Actionable PGx*	CYP2C19: Intermediate metabolizer. One allele showing normal activity and one showing little or no activity.	Individuals with intermediate metabolizer status may have higher plasma concentrations and decreased clearance. Dose reduction may be necessary.	ADR	
Clobazam (Onfi) *FDA drug label: Actionable PGx*	CYP2C19: Intermediate metabolizer. One allele showing normal activity and one showing little or no activity.	Individuals with intermediate metabolizer status may be at an increased risk of adverse drug reaction due to the presence of higher concentrations of clobazam's active metabolite. Consider reducing the initial dose. The FDA approved labeling text for ONFI states that "[t]he initial dose in patients known to be CYP2C19 poor metabolizers should be 5 mg/day. These patients should be titrated initially to 10-20 mg/day, and may be titrated further to a maximum daily dose of 40 mg if tolerated."	ADR	
Phenytoin (Dilantin) *FDA drug label: Actionable PGx*	CYP2C9: Extensive metabolizer. Two alleles showing normal activity.	Typical response is expected; no additional therapeutic recommendations.		

Drug	Finding	Recommendation	Concern	Evidence
Antidementia Agents				
Donepezil (Aricept) *FDA drug label: Actionable PGx*	CYP2D6: Intermediate metabolizer. One allele showing normal function and one showing little or no function.	Individuals with intermediate metabolizer status may be at an increased risk of adverse drug reactions due to reduced metabolic clearance of drug. Insufficient evidence to allow calculation of dose adjustment.	ADR	

Drug	Finding	Recommendation	Concern	Evidence
Antidepressants				
Amitriptyline (Elavil) *FDA drug label: Actionable PGx*	CYP2D6: Intermediate metabolizer. One allele showing normal function and one showing little or no function.	Individuals with intermediate metabolizer status have reduced metabolism of amitriptyline to less active compounds; the resultant higher plasma concentrations will increase the probability of side effects. Consider reducing the recommended starting dose by 25% and monitor plasma concentration or select alternative drug (e.g. citalopram, sertraline).	ADR	
Clomipramine (Anafranil) *FDA drug label: Actionable PGx*	CYP2D6: Intermediate metabolizer. One allele showing normal function and one showing little or no function.	Individuals with intermediate metabolizer status have reduced metabolism to less active compounds; the resultant higher plasma concentrations may increase the probability of side effects. Insufficient evidence to allow calculation of dose adjustment. Monitor (desmethyl) clomipramine plasma concentration.	ADR	
Desipramine (Norpramin) *FDA drug label: Actionable PGx*	CYP2D6: Intermediate metabolizer. One allele showing normal function and one showing little or no function.	Individuals with intermediate metabolizer status have reduced metabolism of tricyclic antidepressants; the resultant higher plasma concentrations may increase the probability of side effects. Monitor plasma concentration or select alternative drug.	ADR	
Doxepin (Deptran) *FDA drug label: Actionable PGx*	CYP2D6: Intermediate metabolizer. One allele showing normal function and one showing little or no function.	Individuals with intermediate metabolizer status have reduced metabolism to less active compounds. Higher plasma concentrations will increase the probability of side effects. Reduce dose by 20%. Adjust maintenance dose in response to (nor)doxepin plasma concentration.	ADR	
Duloxetine (Cymbalta) *FDA drug label: Actionable PGx*	CYP2D6: Intermediate metabolizer. One allele showing normal function and one showing little or no function.	Typical response is expected; no additional therapeutic recommendations.		

Drug	Finding	Recommendation	Concern	Evidence
Imipramine (Tofranil) *FDA drug label: Actionable PGx*	Multigenic: CYP2C19, CYP2D6: CYP2C19: Intermediate metabolizer. One allele showing normal activity and one showing little or no activity.	Multiple results from uncorrelated genes. CYP2C19: Consider alternative therapy; CYP2D6: Recommended dosage adjustment and additional monitoring suggested		
Mirtazapine *FDA drug label: Not established for PGx*	CYP2D6: Intermediate metabolizer. One allele showing normal function and one showing little or no function.	Typical response is expected; no additional therapeutic recommendations.		
Moclobemide (Manerix, Aurorix, Amira, Clobemix, Depnil) *FDA drug label: Not established for PGx*	CYP2C19: Intermediate metabolizer. One allele showing normal activity and one showing little or no activity.	Typical response is expected; no additional therapeutic recommendations.		
Nortriptyline (Pamelor) *FDA drug label: Actionable PGx*	CYP2D6: Intermediate metabolizer. One allele showing normal function and one showing little or no function.	Individuals with intermediate metabolizer status have reduced metabolism of tricyclics to less active compounds when compared to extensive metabolizers; the resultant higher plasma concentrations will increase the probability of side effects. Consider reducing the dose by 40% and monitor nortriptyline 10-hydroxynortriptyline plasma concentrations.	ADR	
Protriptyline (Vivactil) *FDA drug label: Actionable PGx*	CYP2D6: Intermediate metabolizer. One allele showing normal function and one showing little or no function.	Individuals with intermediate metabolizer status have reduced metabolism of tricyclic antidepressants; the resultant higher plasma concentrations may increase the probability of side effects. Monitor plasma concentration or select alternative drug.	ADR	
Trazodone (Oleptro, Desyrel) *FDA drug label: Not established for PGx*	CYP3A4: Extensive metabolizer. Two alleles showing normal function.	Typical response is expected; no additional therapeutic recommendations.		

Drug	Finding	Recommendation	Concern	Evidence
Venlafaxine (Effexor) *FDA drug label: Informative PGx*	CYP2D6: Intermediate metabolizer. One allele showing normal function and one showing little or no function.	Insufficient evidence to allow calculation of dose adjustment. Consider selecting alternative drug (e.g. citalopram, sertraline) or adjust dose to clinical response and monitor (O-desmethyl) venlafaxine plasma concentration.		
Vortioxetine (Brintellix) *FDA drug label: Actionable PGx*	CYP2D6: Intermediate metabolizer. One allele showing normal function and one showing little or no function.	Individuals with intermediate metabolizer status may be at an increased risk of adverse drug reactions due to reduced metabolic clearance and high plasma concentrations of the active compound. Consider reducing the dose.	ADR	
Antidiabetics				
Gliclazide *FDA drug label: Not established for PGx*	CYP2C9: Extensive metabolizer. Two alleles showing normal activity.	Typical response is expected; no additional therapeutic recommendations.		
Glimepiride *FDA drug label: Not established for PGx*	CYP2C9: Extensive metabolizer. Two alleles showing normal activity.	Typical response is expected; no additional therapeutic recommendations.		
Glyburide (Glibenclamide) *FDA drug label: Not established for PGx*	CYP2C9: Extensive metabolizer. Two alleles showing normal activity.	Typical response is expected; no additional therapeutic recommendations.		
Metformin (Glucophage®) *FDA drug label: Not established for PGx*	ATM: Enhanced response	Increased drug efficacy likely.		
Saxagliptin (Onglyza) *FDA drug label: Not established for PGx*	CYP3A4: Extensive metabolizer. Two alleles showing normal function.	Typical response is expected; no additional therapeutic recommendations.		
Tolbutamide (Orinase) *FDA drug label: Not established for PGx*	CYP2C9: Extensive metabolizer. Two alleles showing normal activity.	Typical response is expected; no additional therapeutic recommendations.		

Drug	Finding	Recommendation	Concern	Evidence
Antiemetics				
Ondansetron (Zofran) *FDA drug label: Informative PGx*	CYP2D6: Intermediate metabolizer. One allele showing normal function and one showing little or no function.	Typical response is expected; no additional therapeutic recommendations.		
Tropisetron (Navoban, Setrovel) *FDA drug label: Not established for PGx*	CYP2D6: Intermediate metabolizer. One allele showing normal function and one showing little or no function.	No additional therapeutic recommendations. However, be aware that there is some evidence that individuals with poor metabolizer status may have higher concentrations.		
Antifungals				
Ketoconazole (Nizoral) *FDA drug label: Not established for PGx*	CYP3A4: Extensive metabolizer. Two alleles showing normal function.	Typical response is expected; no additional therapeutic recommendations.		
Voriconazole (Vfend) *FDA drug label: Actionable PGx*	CYP2C19: Intermediate metabolizer. One allele showing normal activity and one showing little or no activity.	Individuals with intermediate metabolizer status may have higher voriconazole exposure. Adjust the dose and monitor for adverse events or lack of efficacy.	ADR & Efficacy	
Antineoplastic Agents				
Methotrexate (Rheumatrex, Trexall) *FDA drug label: Not established for PGx*	MTHFR: Decreased function. One allele showing normal activity and one showing decreased activity.	Individuals with decreased function may be at an increased risk of therapeutic failure and toxicity due to reduced metabolic clearance and increased plasma concentrations. Select alternative drug.	ADR & Efficacy	

Drug	Finding	Recommendation	Concern	Evidence
Antiplatelet Agents				
Clopidogrel *FDA drug label: Actionable PGx*	CYP2C19: Intermediate metabolizer. One allele showing normal activity and one showing little or no activity.	Individuals with intermediate metabolizer status are at an increased risk therapeutic failure due to reduced activation of the prodrug and low plasma concentrations of the active compound. Clopidogrel is not recommended.	Efficacy	
Prasugrel *FDA drug label: Informative PGx*	CYP2C19: Intermediate metabolizer. One allele showing normal activity and one showing little or no activity.	Typical response is expected; no additional therapeutic recommendations.		
Ticagrelor (Brilinta) *FDA drug label: Not established for PGx*	CYP3A4: Extensive metabolizer. Two alleles showing normal function.	Typical response is expected; no additional therapeutic recommendations.		

Drug	Finding	Recommendation	Concern	Evidence
Antipsychotics				
Aripiprazole (Abilify) *FDA drug label: Actionable PGx*	CYP2D6: Intermediate metabolizer. One allele showing normal function and one showing little or no function.	Intermediate metabolizers are at uncertain risk of adverse drug reaction. However, note that for individuals with poor metabolizer status it is recommended to reduce the maximum dose to 10 mg/day (67% of the maximum recommended daily dose).	ADR	
Brexpiprazole (Rexulti) *FDA drug label: Actionable PGx*	CYP2D6: Intermediate metabolizer. One allele showing normal function and one showing little or no function.	Typical response is expected; no additional therapeutic recommendations.		
Clozapine *FDA drug label: Actionable PGx*	CYP2D6: Intermediate metabolizer. One allele showing normal function and one showing little or no function.	Typical response is expected; no additional therapeutic recommendations.		
Flupenthixol *FDA drug label: Not established for PGx*	CYP2D6: Intermediate metabolizer. One allele showing normal function and one showing little or no function.	Typical response is expected; no additional therapeutic recommendations.		
Haloperidol (Haldol) *FDA drug label: Not established for PGx*	CYP2D6: Intermediate metabolizer. One allele showing normal function and one showing little or no function.	Typical response is expected; no additional therapeutic recommendations.		
Iloperidone *FDA drug label: Actionable PGx*	CYP2D6: Intermediate metabolizer. One allele showing normal function and one showing little or no function.	Individuals with intermediate metabolizer status may be at increased risk of adverse events due to increased Iloperidone concentrations. Consider dose reduction based upon assessment of clinical benefit and tolerability.	Efficacy	

Drug	Finding	Recommendation	Concern	Evidence
Olanzapine (Zalasta, Zyprexa) *FDA drug label: Not established for PGx*	CYP2D6: Intermediate metabolizer. One allele showing normal function and one showing little or no function.	Typical response is expected; no additional therapeutic recommendations.		
Perphenazine (Trilafon) *FDA drug label: Actionable PGx*	CYP2D6: Intermediate metabolizer. One allele showing normal function and one showing little or no function.	Individuals with intermediate metabolizer status may be at increased risk of adverse effects due to increased plasma concentrations of perphenazine. Insufficient evidence to allow calculation of dose adjustment. Be alert to adverse reactions.	ADR	
Pimozide (Orap) *FDA drug label: Testing required*	CYP2D6: Intermediate metabolizer. One allele showing normal function and one showing little or no function.	Typical response is expected. For children, the drug label recommends an initial dose of 0.05 mg/kg followed by titration to response up to a maximum of 0.2 mg/kg and not to exceed 10 mg/day. In adults the drug label recommends an initial dose of 1 to 2 mg a day in divided doses followed by titration to response up to a maximum of 0.2 mg/kg/day or 10 mg/day.	ADR	
Quetiapine (Seroquel) *FDA drug label: Not established for PGx*	CYP3A4: Extensive metabolizer. Two alleles showing normal function.	Typical response is expected; no additional therapeutic recommendations.		
Risperidone (Risperdal) *FDA drug label: Informative PGx*	CYP2D6: Intermediate metabolizer. One allele showing normal function and one showing little or no function.	Insufficient evidence to allow calculation of dose adjustment. Consider selecting alternative drug (e.g. quetiapine, olanzapine, clozapine) or being extra alert to adverse drug events and adjusting dose to clinical response.	ADR	
Thioridazine *FDA drug label: Actionable PGx*	CYP2D6: Intermediate metabolizer. One allele showing normal function and one showing little or no function.	Individuals with intermediate metabolizer status are at an increased risk of serious adverse drug reactions due to elevated levels of thioridazine. Select alternative drug.	ADR	

Drug	Finding	Recommendation	Concern	Evidence
Zuclopenthixol *FDA drug label: Not established for PGx*	CYP2D6: Intermediate metabolizer. One allele showing normal function and one showing little or no function.	Individuals with intermediate metabolizer status have decreased metabolism to less active compounds; the resultant increased plasma concentrations may increase the risk of adverse drug reactions. Reduce the standard dose by 25% or select an alternative drug (flupenthixol, quetiapine, olanzapine, clozapine).	ADR	
Anti-Retroviral Agents				
Efavirenz (Sustiva) *FDA drug label: Actionable PGx*	CYP2B6: Extensive metabolizer. Two alleles showing normal activity.	Typical response is expected; no additional therapeutic recommendations.		
Nevirapine (Viramune) *FDA drug label: Not established for PGx*	CYP2B6: Extensive metabolizer. Two alleles showing normal activity.	Typical response is expected; no additional therapeutic recommendations.		
Anxiolytics				
Alprazolam (Xanax, Niravam) *FDA drug label: Not established for PGx*	CYP3A4: Extensive metabolizer. Two alleles showing normal function.	Typical response is expected; no additional therapeutic recommendations.		
Buspirone (Buspar) *FDA drug label: Not established for PGx*	CYP3A4: Extensive metabolizer. Two alleles showing normal function.	Typical response is expected; no additional therapeutic recommendations.		
Clonazepam (Klonopin) *FDA drug label: Not established for PGx*	CYP3A4: Extensive metabolizer. Two alleles showing normal function.	Typical response is expected; no additional therapeutic recommendations.		
Diazepam *FDA drug label: Actionable PGx*	CYP2C19: Intermediate metabolizer. One allele showing normal activity and one showing little or no activity.	Individuals with intermediate metabolizer status may emerge from anesthesia less rapidly due to decreased metabolic clearance. Insufficient evidence to allow calculation of dose adjustment. Be alert to symptoms of excessive drug exposure.	ADR & Efficacy	

Drug	Finding	Recommendation	Concern	Evidence
Beta-3 Adrenergic Agonists				
Mirabegron (Myrbetriq) *FDA drug label: Actionable PGx*	CYP2D6: Intermediate metabolizer. One allele showing normal function and one showing little or no function.	Typical response is expected; no additional therapeutic recommendations.		
Beta Blockers				
Carvedilol (Coreg) *FDA drug label: Actionable PGx*	CYP2D6: Intermediate metabolizer. One allele showing normal function and one showing little or no function.	Typical response is expected; no additional therapeutic recommendations.		
Metoprolol (Lopressor) *FDA drug label: Informative PGx*	CYP2D6: Intermediate metabolizer. One allele showing normal function and one showing little or no function.	Individuals with intermediate metabolizer status have increased risk of adverse drug reactions. For heart failure (indication): select alternative drug (e.g. bisoprolol, carvedilol) or reduce dose by 50%. For other indications: be alert to adverse drug events (e.g. bradycardia, cold extremities) or select alternative drug (e.g. atenolol, bisoprolol).	ADR	
Nebivolol (Bystolic) *FDA drug label: Informative PGx*	CYP2D6: Intermediate metabolizer. One allele showing normal function and one showing little or no function.	Typical response is expected; no additional therapeutic recommendations.		
Propranolol (Inderal) *FDA drug label: Informative PGx*	CYP2D6: Intermediate metabolizer. One allele showing normal function and one showing little or no function.	Typical response is expected; no additional therapeutic recommendations.		

Drug	Finding	Recommendation	Concern	Evidence
Central Monoamine-Depleting Agents				
Tetrabenazine (Xenazine) *FDA drug label: Testing required*	CYP2D6: Intermediate metabolizer. One allele showing normal function and one showing little or no function.	Typical response is expected. The drug label recommends a maximum daily dose of 100 mg and a maximum single dose of 37.5 mg.		
Central Nervous System Agents				
Dextromethorphan-Quinidine (Nuedexta) *FDA drug label: Testing recommended*	CYP2D6: Intermediate metabolizer. One allele showing normal function and one showing little or no function.	Individuals with intermediate metabolizer status may be at an increased risk of adverse events and therapeutic failure. Consider alternative therapy.		
Cholinergic Agonists				
Cevimeline (Evoxac) *FDA drug label: Actionable PGx*	CYP2D6: Intermediate metabolizer. One allele showing normal function and one showing little or no function.	Individuals with intermediate metabolizer status may be at an increased risk of adverse drug reactions due to reduced metabolic clearance and abnormally high plasma concentrations of the active compound. Insufficient evidence to allow calculation of dose adjustment. Cevimeline should be administered with caution.	ADR	
Cholinesterase Inhibitors				
Galantamine (Razadyne, Razadyne ER, Nivalin, Lycoremine, Reminyl) *FDA drug label: Informative PGx*	CYP2D6: Intermediate metabolizer. One allele showing normal function and one showing little or no function.	Typical response is expected; no additional therapeutic recommendations.		
Contraceptives				
Estrogen-containing oral contraceptives *FDA drug label: Not established for PGx*	F5: Two wild-type alleles.	Typical response is expected; no additional therapeutic recommendations.		

Drug	Finding	Recommendation	Concern	Evidence
EGFR Inhibitors				
Gefitinib (Iressa) *FDA drug label: Testing required*	CYP2D6: Intermediate metabolizer. One allele showing normal function and one showing little or no function.	Typical response is expected; no additional therapeutic recommendations.		
Endocrine-Metabolic Agents				
Eliglustat *FDA drug label: Testing required*	CYP2D6: Intermediate metabolizer. One allele showing normal function and one showing little or no function.	Typical response is expected. The drug label recommends a dose of 84 mg twice daily.		
Hypnotics				
Eszopiclone (Lunesta) *FDA drug label: Not established for PGx*	CYP3A4: Extensive metabolizer. Two alleles showing normal function.	Typical response is expected; no additional therapeutic recommendations.		
Immunosuppressants				
Cyclosporine (Gengraf, Neoral) *FDA drug label: Not established for PGx*	CYP3A4: Extensive metabolizer. Two alleles showing normal function.	Typical response is expected; no additional therapeutic recommendations.		
Sirolimus (Rapamune) *FDA drug label: Not established for PGx*	CYP3A4: Extensive metabolizer. Two alleles showing normal function.	Typical response is expected; no additional therapeutic recommendations.		
Tacrolimus (Prograf, Hecoria) *FDA drug label: Not established for PGx*	CYP3A5: Two alleles showing little or no activity.	Individuals with poor metabolizer status have higher dose-adjusted trough concentrations of tacrolimus; the resultant increased concentrations may increase the probability of pharmacotherapy success. Consider initiating therapy with the recommended starting dose. In liver transplant patients, donor genotype should be considered as well as the recipient's.		

Drug	Finding	Recommendation	Concern	Evidence
Muscle Relaxants				
Carisoprodol (Soma) *FDA drug label: Actionable PGx*	CYP2C19: Intermediate metabolizer. One allele showing normal activity and one showing little or no activity.	Individuals with intermediate metabolizer status may be at an increased risk of adverse drug reactions due to reduced carisoprodol metabolism. Carisoprodol should be administered with caution.	ADR	
Non-drug				
ApoE	ApoE: ε4 is often associated with a potential change in LDL cholesterol and plasma triglyceride levels.	There is a potential increased risk of cardiovascular disease and atherosclerosis.		
COMT(Val158Met)	COMT(Val158Met): Increased function. Two alleles with increased activity.	Increased function. Two alleles with increased activity.		
CYP1A2	CYP1A2: Ultra-rapid metabolizer. Two alleles showing increased activity.	No additional therapeutic recommendations.		
CYP2B6	CYP2B6: Extensive metabolizer. Two alleles showing normal activity.	No additional therapeutic recommendations.		
DPYD	DPYD: Extensive metabolizer. Two alleles showing normal activity.	Typical response is expected; no additional therapeutic recommendations.		

Drug	Finding	Recommendation	Concern	Evidence
Nonsteroidal Anti-Inflamatory Drugs (NSAIDs)				
Celecoxib (Celebrex) *FDA drug label: Actionable PGx*	CYP2C9: Extensive metabolizer. Two alleles showing normal activity.	Typical response is expected; no additional therapeutic recommendations.		
Diclofenac (Cataflam) *FDA drug label: Not established for PGx*	CYP2C9:rs1057910: Two alleles showing normal activity.	Typical response is expected; no additional therapeutic recommendations.		
Flurbiprofen (Ocufen) *FDA drug label: Actionable PGx*	CYP2C9: Extensive metabolizer. Two alleles showing normal activity.	Typical response is expected; no additional therapeutic recommendations.		
Ibuprofen (Motrin, Advil) *FDA drug label: Not established for PGx*	CYP2C9: Extensive metabolizer. Two alleles showing normal activity.	Typical response is expected; no additional therapeutic recommendations.		
Lornoxicam (Xefo) *FDA drug label: Not established for PGx*	CYP2C9: Extensive metabolizer. Two alleles showing normal activity.	Typical response is expected; no additional therapeutic recommendations.		
Meloxicam (Mobic) *FDA drug label: Not established for PGx*	CYP2C9: Extensive metabolizer. Two alleles showing normal activity.	Typical response is expected; no additional therapeutic recommendations.		
Piroxicam (Feldene) *FDA drug label: Actionable PGx*	CYP2C9: Extensive metabolizer. Two alleles showing normal activity.	Typical response is expected; no additional therapeutic recommendations.		

Drug	Finding	Recommendation	Concern	Evidence
Opioids				
Buprenorphine (Butrans, Buprenex) *FDA drug label: Not established for PGx*	CYP3A4: Extensive metabolizer. Two alleles showing normal function.	Typical response is expected; no additional therapeutic recommendations.		
Codeine *FDA drug label: Actionable PGx*	CYP2D6: Intermediate metabolizer. One allele showing normal function and one showing little or no function.	Individuals with intermediate metabolizer status have reduced formation of morphine following codeine administration; the resultant decreased morphine plasma concentrations leads insufficient pain relief. Be alert to lack of insufficient pain relief.	Efficacy	
Fentanyl (Duragesic, Sublimaze) *FDA drug label: Not established for PGx*	CYP3A4: Extensive metabolizer. Two alleles showing normal function.	Typical response is expected; no additional therapeutic recommendations.		
Hydrocodone *FDA drug label: Not established for PGx*	CYP2D6: Intermediate metabolizer. One allele showing normal function and one showing little or no function.	Typical response is expected; no additional therapeutic recommendations.		
Oxycodone (Oxycontin) *FDA drug label: Not established for PGx*	CYP2D6: Intermediate metabolizer. One allele showing normal function and one showing little or no function.	Individuals with intermediate metabolizer status are at risk of potentially reduced efficacy; consider alternative therapy. Insufficient evidence to allow calculation of dose adjustment. Select alternative drug (not tramadol or codeine) or be alert to symptoms of insufficient pain relief.	Efficacy	
Oxycodone (CYP3A5) (Oxycontin) *FDA drug label: Not established for PGx*	CYP3A5: Two alleles showing little or no activity.	In a preliminary study, individuals with poor metabolizers status have a significantly higher opioid escalation index compared to normal (extensive) metabolizers. Though the impact of metabolizer status at CYP3A5 on pain relief is currently unknown, consider reducing the initial dose. There does not appear to be an effect of this metabolizer status on the incidence of drowsiness.	ADR & Efficacy	

Drug	Finding	Recommendation	Concern	Evidence
Tramadol (Ultracet, Ultram) *FDA drug label: Actionable PGx*	CYP2D6: Intermediate metabolizer. One allele showing normal function and one showing little or no function.	Individuals with intermediate metabolizer status have decreased metabolism to more active compounds; the resultant decreased plasma concentrations may increase the probability of pharmacotherapy failure. Consider dose increase. If response is still inadequate; select alternative drug (not oxycodone or codeine) or be alert to symptoms of insufficient pain relief.	Efficacy	

Drug	Finding	Recommendation	Concern	Evidence
Proton Pump Inhibitors (PPIs)				
Dexlansoprazole (Dexilant, Kapidex) *FDA drug label: Actionable PGx*	CYP2C19: Intermediate metabolizer. One allele showing normal activity and one showing little or no activity.	Individuals with intermediate metabolizer status have decreased metabolism to less active compounds; the resultant increased concentrations may increase drug efficacy. Individual is expected to respond well to PPI treatment; no additional therapeutic recommendations.	Efficacy	
Esomeprazole (Nexium) *FDA drug label: Actionable PGx*	CYP2C19: Intermediate metabolizer. One allele showing normal activity and one showing little or no activity.	Individuals with intermediate metabolizer status have decreased metabolism to less active compounds; the resultant increased concentrations may increase drug efficacy. Individual is expected to respond well to PPI treatment; no additional therapeutic recommendations.	Efficacy	
Lansoprazole (Prevacid) *FDA drug label: Informative PGx*	CYP2C19: Intermediate metabolizer. One allele showing normal activity and one showing little or no activity.	Individuals with intermediate metabolizer status have decreased metabolism to less active compounds; the resultant increased concentrations may increase drug efficacy. Individual is expected to respond well to PPI treatment; no additional therapeutic recommendations.	Efficacy	
Omeprazole (Prilosec, Zegerid) *FDA drug label: Actionable PGx*	CYP2C19: Intermediate metabolizer. One allele showing normal activity and one showing little or no activity.	Individuals with intermediate metabolizer status have decreased metabolism to less active compounds; the resultant increased concentrations may increase drug efficacy. Individual is expected to respond well to PPI treatment; no additional therapeutic recommendations.	Efficacy	
Pantoprazole (Protonix) *FDA drug label: Actionable PGx*	CYP2C19: Intermediate metabolizer. One allele showing normal activity and one showing little or no activity.	Individuals with intermediate metabolizer status have decreased metabolism to less active compounds; the resultant increased concentrations may increase drug efficacy. Individual is expected to respond well to PPI treatment; no additional therapeutic recommendations.	Efficacy	
Rabeprazole (Aciphex) *FDA drug label: Actionable PGx*	CYP2C19: Intermediate metabolizer. One allele showing normal activity and one showing little or no activity.	Individuals with intermediate metabolizer status have decreased metabolism to less active compounds; the resultant increased concentrations may increase drug efficacy. Individual is expected to respond well to PPI treatment; no additional therapeutic recommendations.	Efficacy	

Drug	Finding	Recommendation	Concern	Evidence
Selective Serotonin Reuptake Inhibitors (SSRIs)				
Citalopram (Celexa) *FDA drug label: Actionable PGx*	CYP2C19: Intermediate metabolizer. One allele showing normal activity and one showing little or no activity.	Individuals with intermediate metabolizer status may have higher plasma concentrations and decreased clearance. Dose reduction may be necessary.	ADR	
Escitalopram (Lexapro) *FDA drug label: Actionable PGx*	CYP2C19: Intermediate metabolizer. One allele showing normal activity and one showing little or no activity.	Individuals with intermediate metabolizer status may have higher plasma concentrations and decreased clearance. Dose reduction may be necessary.	ADR	
Fluoxetine (Prozac) *FDA drug label: Informative PGx*	CYP2D6: Intermediate metabolizer. One allele showing normal function and one showing little or no function.	Typical response is expected; no additional therapeutic recommendations.		
Fluvoxamine (Luvox) *FDA drug label: Actionable PGx*	CYP2D6: Intermediate metabolizer. One allele showing normal function and one showing little or no function.	Individuals with intermediate metabolizer status may be at an increased risk of adverse drug reactions due to reduced metabolic clearance. Insufficient evidence to allow calculation of dose adjustment. Be alert to adverse reactions.	ADR	
Paroxetine (Paxil) *FDA drug label: Informative PGx*	CYP2D6: Intermediate metabolizer. One allele showing normal function and one showing little or no function.	Individuals with intermediate metabolizer status may have increased plasma concentrations/ decreased clearance of paroxetine. However, an association with treatment response or severity of side effects is not conclusive.	ADR	
Sertraline (Zoloft) *FDA drug label: Not established for PGx*	CYP2C19: Intermediate metabolizer. One allele showing normal activity and one showing little or no activity.	Individuals with intermediate metabolizer status may have higher plasma concentrations and decreased clearance. Insufficient evidence to allow calculation of dose adjustment. Be extra alert to adverse drug reactions (e.g. nausea; vomiting; diarrhea).	ADR	

Drug	Finding	Recommendation	Concern	Evidence
Statins				
Atorvastatin (Lipitor, Caduet) *FDA drug label: Not established for PGx*	CYP3A4: Extensive metabolizer. Two alleles showing normal activity.	Typical response is expected; no additional therapeutic recommendations.		
Simvastatin (Zocor) *FDA drug label: Informative PGx*	SLCO1B1: Intermediate liver uptake activity.	Individuals with intermediate SLCO1B1 liver uptake activity have a moderately increased risk of myopathy when taking a 40 mg/day or higher dose of simvastatin. A reduced dosage or alternate statin drug should be considered.	ADR	
Vesicular monoamine transporter 2 inhibitor				
Deutetrabenazine (Austedo) *FDA drug label: Actionable PGx*	CYP2D6: Intermediate metabolizer. One allele showing normal function and one showing little or no function.	Individuals with intermediate metabolizer status may be at increased risk of QT prolongation due to increased levels of the active metabolite. The drug label for poor metabolizer recommends a maximum daily dose of 36 mg and a maximum single dose of 18 mg.	ADR	

Clinical Evidence Levels

Strong

- 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.

Patient Information Card

This card contains an abbreviated genetic summary.
It is not intended as a replacement for the complete GeneDose™ report.

NOVALAB Reference Medical Lab

Patient: DOE, JANE
DOB: 1950-12-25
Sample ID: 20P00000

Pharmacogenomic Summary

ApoE	ε3|ε4	See full GeneDose report
Factor V Leiden	Normal	See full GeneDose report
MTHFR (A1298C)	Normal	See full GeneDose report
MTHFR (C677T)	Heterozygous	See full GeneDose report
Prothrombin (F2)	Normal	See full GeneDose report

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This card shows information about your genetics that relate to drug metabolism. Show to your doctors before being prescribed new medications.

ATM	A|C	Increased likelihood of treatment success when taking metformin
COMT(Val158Met)	G|G	Multiple statuses; see per-drug detail
CYP1A2	*1F|*1F	Ultrarapid metabolizer
CYP2B6	*1A|*1A	Extensive metabolizer
CYP2C19	*1|*2	Intermediate metabolizer
CYP2C9	*1|*1	Extensive metabolizer
CYP2D6	*2B|*4A or *4K|*39; or *2A|*4A	Intermediate metabolizer
CYP3A4	*1A|*1A	Multiple statuses; see per-drug detail
CYP3A5	*3A|*3A; or *3C|*3C; or *3A|*3C	Poor metabolizer
DPYD	*1|*1	Normal function
MTHFR	GT|AT	Reduced function
SLCO1B1	*1|*5	Intermediate liver uptake activity
VKORC1	*1|*2	Reduced (with respect to Warfarin)

↑ Fold Here