PRECISION GENETICS

Sample Org
123 Street Street Greenville, SC 29615

PATIENT INFORMATION	
NAME:	test14 test14
DOB:	04/29/1962
SEX:	Female

SPECIMEN DETAILS	
SAMPLE ID:	PGT-24-001-14
SPECIMEN TYPE:	None
COLLECTION DATE:	02/21/2024
RECEIVED DATE:	02/23/2024
REPORT DATE:	05/16/2024

PROVIDER INFORMATION	
PROVIDER:	LOREN KIDD
FACILITY:	Medical Office

Comprehensive PGx Express 120 Report

1 Current Patient Medications

Note that either no information was provided regarding current medications for this patient, or that pharmacogenomics interpretation is not available for the current medications at this time. It is highly recommend to consult a physician or a pharmacist to determine the pharmacogenomics implications when the patient is prescribed new medication.

Unrecognized Medications: None
Outside of Scope Medications: Amitriptyline / Elavil
Defined as those that do not have PGx currently have pharmacogenetic guidance available to report.

2 Risk Management

Hyperuricemia and Gout
Normal Risk of Gout

The patient carries two copies of ABCG2 rs2231142 C allele.
The ABCG2 rs2231142 C allele is associated with normal ABCG2 activity and subsequent normal renal elimination of uric acid. The patient's genotype is associated with a normal risk of hyperuricemia and gout.
No action is needed for this patient unless other genetic or non-genetic risk factors are present.

Antipsychotic-Induced Tardive Dyskinesia
Moderate Risk of Antipsychotic-Induced Tardive Dyskinesia

Moderate risk for antipsychotic-induced tardive dyskinesia.
The patient carries one copy of the Taq1A variant (heterozygous for the A1 allele).
The genotype results predict that the patient may have reduced dopamine receptor DRD2 density and hypodopaminergic functioning. The patient has moderate risk for tardive dyskinesia when treated with antipsychotics.
Monitor the patient for any signs of tardive dyskinesia.

Antipsychotic-Induced Hyperprolactinemia
Moderate Risk of Antipsychotic-induced Hyperprolactinemia

Moderate risk of antipsychotic-induced hyperprolactinemia.
The patient carries one copy of the Taq1A variant (heterozygous for the A1 allele).
The genotype results predict that the patient may have reduced dopamine receptor DRD2 density and hypodopaminergic functioning. The patient has moderate risk of hyperprolactinemia when treated with antipsychotics.
Monitor patient closely for signs of hyperprolactinemia. An evaluation of the risk-benefit profile of the antipsychotic medication may be required.

Antipsychotic-Induced Weight Gain
Moderate Risk of Antipsychotic-Induced Weight Gain

Moderate risk for antipsychotic-induced weight gain.
The patient carries one copy of the Taq1A variant (heterozygous for the A1 allele).
The genotype results predict that the patient may have reduced dopamine receptor DRD2 density and hypodopaminergic functioning. The patient has moderate risk for weight gain when treated with antipsychotics.
Monitor patient closely for signs of weight gain.

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Platelet Hyperactivity

Normal Response to Aspirin

Normal Platelet Reactivity

The patient is negative for the ITGB3 176T>C (Leu59Pro) mutation. The genotype for the integrin β3 gene is wild-type, which is the most common genotype in the general population.

The wild-type genotype results confers a "normal" platelet reactivity, and is not associated with a resistance to the antithrombotic effects of aspirin. However, because the variability in response to antiplatelet drugs is multifactorial and not caused by single gene mutations, testing for the ITGB3 mutation alone should not be used as a diagnostic tool.

Hyperhomocysteinemia - Depression

No Increased Risk of Hyperhomocysteinemia

The patient does not carry the MTHFR c.665C>T variant. MTHFR enzyme activity is normal.

Patients diagnosed with depression often have low folate levels and homocysteine is a highly sensitive marker of folate status. Functional folate deficiency is indicated by elevated homocysteine. With a normal MTHFR activity, this patient can process folate normally and is unlikely to have elevated plasma levels of homocysteine.

Patients diagnosed with depression: as lower folate levels are associated with poorer antidepressant response, and baseline levels of folate within the normal range predict antidepressant response, testing for homocysteine levels and serum folate levels may be informative for this patient before prescribing methylfolate as an antidepressant-augmenting agent.

Hyperhomocysteinemia - Thrombosis

No Increased Risk of Hyperhomocysteinemia

The patient carries two copies of MTHFR c.1286A>C variant (homozygous) and no MTHFR c.665C>T variant. MTHFR enzyme activity is reduced (60% of normal activity).

The patient's reduced MTHFR activity is a not a risk factor for hyperhomocysteinemia. Unless other risk factors are present, the patient is not expected to have an increased risk for venous thromboembolism (VTE).

3 Potentially Impacted Medications

Medications are binned according to their respective therapeutic class and specialty, as well as the predicted impact of the patient's genotypes. The drugs that appear in this table are based solely on the patient's genetic results. Please note that there are available alternative medications that do not have PGx guidance and are not included within this report.

Category	Drug Class	Standard Precautions	Caution	Alternatives Recommended
Anticancer Agents	Anti-Estrogens			Tamoxifen (Nolvadex®, Soltamox®)
	Antifolates	Methotrexate (Trexall®)		
	Protein Kinase Inhibitors	Erdafitinib (Balversa®) Gefitinib (Iressa®)		
	Taxanes	Paclitaxel (Taxol®, Abraxane®)		
	Thiopurines		Azathioprine (Azasan®, Imuran®) Mercaptopurine (Purinethol®, Purixan®) Thioguanine (Tabloid®)	
Antihistamines	Histamine (H1) Receptor Antagonists		Meclizine (Antivert®)	
Cardiovascular	Angiotensin II Receptor Antagonists	Azilsartan (Edarbi®, Edarbyclor®) Irbesartan (Avapro®) Losartan (Cozaar®, Hyzaar®)		
	Antianginal Agents	Ranolazine (Ranexa®)		
	Antiarrhythmics		Flecainide (Tambocor®) Mexiletine (Mexitil®) Propafenone (Rythmol®)	
	Anticoagulants	Warfarin (Coumadin®)		
	Antiplatelets			Clopidogrel (Plavix®)
	Beta Blockers	Carvedilol (Coreg®) Nebivolol (Bystolic®) Propranolol (Inderal®)	Metoprolol (Lopressor®) Timolol (Blocadren®)	
	Cardiac myosin inhibitor		Mavacamten (Camzyos®)	
	Diuretics	Torsemide (Demadex®)		

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Category	Drug Class	Standard Precautions	Caution	Alternatives Recommended
	Statins	Atorvastatin (Lipitor®) Fluvastatin (Lescol®) Lovastatin (Mevacor®, Altoprev®, Advicor®) Pitavastatin (Livalo®) Pravastatin (Pravachol®) Rosuvastatin (Crestor®) Simvastatin (Zocor®)		
Diabetes	**Meglitinides**	Nateglinide (Starlix®) Repaglinide (Prandin®, Prandimet®)		
	Thiazolidinediones	Pioglitazone (Actos®, Oseni®) Rosiglitazone (Avandia®)		
Gastrointestinal	**Antiemetics**	Dolasetron (Anzemet®) Dronabinol (Marinol®) Fosnetupitant / Palonosetron (Akynzeo-IV®) Netupitant / Palonosetron (Akynzeo-oral®) Palonosetron (Aloxi®)	Granisetron (Sancuso®, Sustol®) Metoclopramide (Reglan®) Ondansetron (Zofran®, Zuplenz®)	
	Proton Pump Inhibitors	Dexlansoprazole (Dexilant®, Kapidex®) Esomeprazole (Nexium®) Lansoprazole (Prevacid®) Omeprazole (Prilosec®) Pantoprazole (Protonix®) Rabeprazole (Aciphex®)		
Gaucher Disease	**Endocrine-Metabolic Agents**	Eliglustat (Cerdelga®)		
Gynecology	**Endometriosis Pain Agents**	Elagolix (Orilissa®)		
Infections	**Anti-HIV Agents**	Efavirenz (Sustiva®)		
	Antifungals	Voriconazole (Vfend®)		
Multiple Sclerosis	**Disease-Modifying Agents**	Siponimod (Mayzent®)		
Pain	**Muscle Relaxants**	Carisoprodol (Soma®)	Tizanidine (Zanaflex®)	
	NSAIDs	Celecoxib (Celebrex®) Flurbiprofen (Ansaid®) Ibuprofen (Advil®, Motrin®) Meloxicam (Mobic®) Piroxicam (Feldene®)		

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FACILITY: Medical Office

Category	Drug Class	Standard Precautions	Caution	Alternatives Recommended
	Opioids	Dihydrocodeine (Synalgos-DC®) Fentanyl (Actiq®) Methadone (Dolophine®) Morphine (MS Contin®) Oliceridine (Olinvyk) Oxycodone (Percocet®, Oxycontin®)	Benzhydrocodone (Apadaz®) Codeine (Codeine; Fioricet® with Codeine) Hydrocodone (Vicodin®) Tramadol (Ultram®)	
Psychotropic	**Anti-ADHD Agents**	Amphetamine (Adderall®, Evekeo®) Dextroamphetamine (Dexedrine®) Lisdexamfetamine (Vyvanse®) Viloxazine (Qelbree®)	Atomoxetine (Strattera®) Dexmethylphenidate (Focalin®) Methylphenidate (Ritalin®, Aptensio XR®, Concerta®, Metadate ER®, Quillivant ER®)	
	Antiaddictives	Lofexidine (Lucemyra®)	Bupropion (Wellbutrin®, Zyban®, Aplenzin®, Contrave®) Naltrexone (Vivitrol®, Contrave®)	
	Anticonvulsants	Brivaracetam (Briviact®) Fosphenytoin (Cerebyx®) Phenytoin (Dilantin®)	Phenobarbital (Luminal®) Primidone (Mysoline®) Zonisamide (Zonegran®)	
	Antidementia Agents	Donepezil (Aricept®) Galantamine (Razadyne®)		
	Antidepressants	Desvenlafaxine (Pristiq®) Fluoxetine (Prozac®, Sarafem®) Nefazodone (Serzone®) Venlafaxine (Effexor®)	Amitriptyline (Elavil®) Amoxapine (Amoxapine®) Citalopram (Celexa®) Clomipramine (Anafranil®) Desipramine (Norpramin®) Doxepin (Silenor®) Escitalopram (Lexapro®) Fluvoxamine (Luvox®) Imipramine (Tofranil®) Maprotiline (Ludiomil®) Nortriptyline (Pamelor®) Paroxetine (Paxil®, Brisdelle®) Protriptyline (Vivactil®) Sertraline (Zoloft®) Trimipramine (Surmontil®) Vortioxetine (Trintellix®)	
	Antipsychotics	Aripiprazole (Abilify®, Aristada®) Brexpiprazole (Rexulti®) Chlorpromazine (Thorazine®) Haloperidol (Haldol®) Paliperidone (Invega®) Pimozide (Orap®) Risperidone (Risperdal®)	Clozapine (Clozaril®) Iloperidone (Fanapt®) Olanzapine (Zyprexa®) Perphenazine (Trilafon®)	Thioridazine (Mellaril®)

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Category	Drug Class	Standard Precautions	Caution	Alternatives Recommended
	Benzodiazepines	Clobazam (Onfi®) Diazepam (Valium®)	Lorazepam (Ativan®) Oxazepam (Serax®)	
	Other Neurological Agents	Deutetrabenazine (Austedo®) Dextromethorphan / Quinidine (Nuedexta®) Flibanserin (Addyi®) Valbenazine (Ingrezza®)	Tetrabenazine (Xenazine®)	
Rheumatology	**Anti-Hyperuricemics and Anti-Gout Agents**	Allopurinol (Zyloprim®, Lopurin®, Aloprim®)		
	Immunomodulators		Leflunomide (Arava®)	
	Other Antirheumatic Agents		Sulfasalazine (Azulfidine®, Sulfazine®)	
Sjogren's Syndrome	**Cholinergic Agonists**	Cevimeline (Evoxac®)		
Sleep Disorder Agents	**Narcoleptic Agents**	Pitolisant (Wakix®)		
Transplantation	**Immunosuppressants**	Tacrolimus (Prograf®)		
Urologicals	**Alpha-Blockers for Benign Prostatic Hyperplasia**	Tamsulosin (Flomax®)		
	Antispasmodics for Overactive Bladder	Darifenacin (Enablex®) Fesoterodine (Toviaz®) Mirabegron (Myrbetriq®) Tolterodine (Detrol®)		

4 Dosing Guidance

Clopidogrel
Plavix®

Reduced Exposure to Clopidogrel Active Metabolite — ACTIONABLE

CYP2C19: Intermediate Metabolizer

The patient's genotype is associated with possible decreased clopidogrel exposure. Patients may be at an increased risk for adverse cardiac and cerebrovascular events.

ACS, PCI, and Neurovascular Indications:

Consider an alternative such as prasugrel (contraindicated in TIA/stroke) or ticagrelor. In patients with ACS or PCI, if clopidogrel cannot be avoided, alternative dosing strategies exist and may be considered.

- Plavix [package insert]. Bridgewater, NJ: Bristol-Myers Squibb/Sanofi Pharmaceuticals Partnership; 2021.
- Lee CR, Luzum JA, Sangkuhl K, Gammal RS, Sabatine MS, Stein CM, Kisor DF, Limdi NA, Lee YM, Scott SA, Hulot JS, Roden DM, Gaedigk A, Caudle KE, Klein TE, Johnson JA, Shuldiner AR. Clinical Pharmacogenetics Implementation Consortium Guideline for CYP2C19 Genotype and Clopidogrel Therapy: 2022 Update. Clin Pharmacol Ther 2022 Jan;():.

Tamoxifen
Nolvadex®, Soltamox®

Decreased Response to Tamoxifen — INFORMATIVE

CYP2D6: Intermediate Metabolizer

Adjuvant treatment of estrogen receptor-positive breast cancer: based on the CYP2D6 genotype results, this patient is expected to have low endoxifen (active metabolite of tamoxifen) concentrations. This is associated with a reduced response to this drug and poor treatment outcomes.

Consider alternative hormonal therapy such as an aromatase inhibitor for postmenopausal women or an aromatase inhibitor along with ovarian function suppression in premenopausal women.

If aromatase inhibitors are contraindicated, a higher FDA approved dose of tamoxifen (40 mg/day) can be considered, although a higher dose increases but does not normalize endoxifen concentrations. Consider avoiding the co-administration of this drug with strong, moderate or weak CYP2D6 inhibitors. An increased risk of thromboembolic events is associated with tamoxifen therapy. The risks and benefits of this drug should be carefully considered in women with a history of thromboembolic events or with other coexisting risk factors for thrombosis.

- Goetz MP, Sangkuhl K, Guchelaar HJ, Schwab M, Province M, Whirl-Carrillo M, Symmans WF, McLeod HL, Ratain MJ, Zembutsu H, Gaedigk A, van Schaik RH, Ingle JN, Caudle KE, Klein TE. Clinical Pharmacogenetics Implementation Consortium (CPIC) Guideline for CYP2D6 and Tamoxifen Therapy. Clin Pharmacol Ther 2018 05;103(5):770-777.

Thioridazine
Mellaril®

Increased Sensitivity to Thioridazine — ACTIONABLE

CYP2D6: Intermediate Metabolizer

Reduced cytochrome CYP2D6 activity results in elevated plasma levels of thioridazine, would be expected to augment the prolongation of the QTc interval associated with thioridazine, and may increase the risk of serious, potentially fatal, cardiac arrhythmias, such as Torsades de pointes-type arrhythmias. Such an increased risk may result also from the additive effect of coadministering thioridazine with other agents that prolong the QTc interval. Therefore, thioridazine is contraindicated in patients with reduced levels of CYP2D6 activity.

- Dorado P, Peñas-LLedó EM, de la Rubia A, LLerena A. Relevance of CYP2D6 -1584C>G polymorphism for thioridazine:mesoridazine plasma concentration ratio in psychiatric patients. Pharmacogenomics 2009 Jul;10(7):1083-9.
- Berecz R, de la Rubia A, Dorado P, Fernández-Salguero P, Dahl ML, LLerena A. Thioridazine steady-state plasma concentrations are influenced by tobacco smoking and CYP2D6, but not by the CYP2C9 genotype. Eur J Clin Pharmacol 2003 May;59(1):45-50.
- LLerena A, Berecz R, de la Rubia A, Dorado P. QTc interval lengthening is related to CYP2D6 hydroxylation capacity and plasma concentration of thioridazine in patients. J Psychopharmacol 2002 Dec;16(4):361-4.

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Amitriptyline
Elavil®

Increased Amitriptyline Exposure
ACTIONABLE

CYP2D6: Intermediate Metabolizer

The patient is predicted to be a CYP2D6 intermediate metabolizer which is likely to result in decreased metabolism of amitriptyline to less active compounds and a subsequent increase in amitriptyline exposure leading to side effects.

Psychiatric Conditions: Consider a 25% reduction of the recommended dose and use therapeutic drug monitoring to guide dose adjustments.

Neuropathic Pain: Amitriptyline therapy can be prescribed according to standard recommended dosage and administration when lower doses are considered. If higher doses are warranted, consider a 25% reduction of the recommended dose and monitor patient for side effects.

- Hicks JK, Sangkuhl K, Swen JJ, Ellingrod VL, Müller DJ, Shimoda K, Bishop JR, Kharasch ED, Skaar TC, Gaedigk A, Dunnenberger HM, Klein TE, Caudle KE, Stingl JC. Clinical pharmacogenetics implementation consortium guideline (CPIC) for CYP2D6 and CYP2C19 genotypes and dosing of tricyclic antidepressants: 2016 update. Clin Pharmacol Ther 2017 07;102(1):37-44.

Increased Amitriptyline Exposure
ACTIONABLE

CYP2D6: Intermediate Metabolizer

CYP2C19: Intermediate Metabolizer

The patient's reduced CYP2D6 activity is likely to result in decreased metabolism of amitriptyline to less active compounds and a subsequent increase in amitriptyline exposure leading to side effects.

Psychiatric Conditions: Consider a 25% reduction of the recommended dose and use therapeutic drug monitoring to guide dose adjustments.

Neuropathic Pain: Amitriptyline can be prescribed according to standard recommended dosage and administration when lower doses are considered. If higher doses are warranted, consider a 25% reduction of the recommended starting dose and monitor patient for side effects.

- Hicks JK, Sangkuhl K, Swen JJ, Ellingrod VL, Müller DJ, Shimoda K, Bishop JR, Kharasch ED, Skaar TC, Gaedigk A, Dunnenberger HM, Klein TE, Caudle KE, Stingl JC. Clinical pharmacogenetics implementation consortium guideline (CPIC) for CYP2D6 and CYP2C19 genotypes and dosing of tricyclic antidepressants: 2016 update. Clin Pharmacol Ther 2017 07;102(1):37-44.

Amoxapine
Amoxapine®

Possible Increased Amoxapine Exposure
INFORMATIVE

CYP2D6: Intermediate Metabolizer

Like other tricyclic and tetracyclic antidepressants, amoxapine is metabolized by CYP2D6. However, the overall contribution of this enzyme in the metabolism of this drug is not well documented. Decreased CYP2D6 activity may result in higher amoxapine concentrations potentially leading to higher adverse events. There are no established dosing adjustments for patients with decreased CYP2D6 function; therapy must be initiated cautiously and adjusted according to the patient's response.

- AMOXAPINE- amoxapine tablet [package insert]. Parsippany, NJ: Watson Pharma, Inc. https://dailymed.nlm.nih.gov/dailymed/archives/fdaDrugInfo.cfm?archiveid=151241. Rev Jun 2014.

Atomoxetine
Strattera®

Possibly Increased Atomoxetine Exposure
ACTIONABLE

CYP2D6: Intermediate Metabolizer

The genotype result indicates that the patient may have an insufficient response due to inadequate drug exposure following standard dosing as compared with poor metabolizers.

Consider the following dosing strategy:

- Initiate treatment at 40 mg/day, then increase to 80 mg/day after 3 days.
- If after 2 weeks, optimal clinical response is not observed and adverse events are not present, consider a dose increase to 100 mg/day.
- If after an additional 2 weeks, optimal clinical response is not observed, consider therapeutic drug monitoring 1-2 hours post dose. If the plasma concentration is < 200 ng/mL, consider a proportional dose increase to approach 400 ng/mL. Doses > 100 mg/day may be needed to achieve a target therapeutic concentration (therapeutic range: 200-1,000 ng/mL). Note: doses above 120 mg/day have not been evaluated.

- Brown JT, Bishop JR, Sangkuhl K, Nurmi EL, Mueller DJ, Dinh JC, Gaedigk A, Klein TE, Caudle KE, McCracken JT, de Leon J, Leeder JS. Clinical Pharmacogenetics Implementation Consortium Guideline for Cytochrome P450 (CYP)2D6 Genotype and Atomoxetine Therapy. Clin Pharmacol Ther 2019 Jul;106(1):94-102.
- Atomoxetine [package insert]. Parsippany, NJ: Teva Pharmaceuticals; 2022.

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Azathioprine
Azasan®, Imuran®

Increased Risk of Myelotoxicity
ACTIONABLE

TPMT: Poor or Intermediate Metabolizer
NUDT15: Normal Metabolizer

The TPMT genotype results for this patient are indicative of a *1/*3A predicting intermediate TPMT activity. However, there is a small risk (<1 in 100,000) that this patient's genotype is instead *3B/*3C which would predict a low TPMT activity. A TPMT phenotype test could distinguish between these possible phenotypes.

Evidence shows that 30 to 60% of patients with these genotype results experience severe leukopenia, neutropenia or myelosuppression with standard doses of azathioprine.

Nonmalignant indications

Therapy initiation: if normal starting dose is 2-3mg/kg/day, consider decreasing start dose to 30-80% of normal dose and adjust subsequent doses based on disease-specific guidelines and/or myelosuppression, as needed. Allow 2-4 weeks to reach steady state after each dose adjustment. Alternative medications may also be considered.

Malignant indications

Therapy initiation: if normal starting dose is 2-3mg/kg/day, consider decreasing start dose to 30-80% of normal dose and adjust subsequent doses based on disease-specific guidelines and myelosuppression. Allow 2-4 weeks to reach steady state after each dose adjustment.

These genotype results cannot be used to assess the patient's risk of thiopurine-related pancreatitis or hepatotoxicity.

- Relling MV, Schwab M, Whirl-Carrillo M, Suarez-Kurtz G, Pui CH, Stein CM, Moyer AM, Evans WE, Klein TE, Antillon-Klussmann FG, Caudle KE, Kato M, Yeoh AEJ, Schmiegelow K, Yang JJ. Clinical Pharmacogenetics Implementation Consortium Guideline for Thiopurine Dosing Based on TPMT and NUDT15 Genotypes: 2018 Update. Clin Pharmacol Ther 2019 May;105(5):1095-1105.

Benzhydrocodone
Apadaz®

Possible Decreased Exposure to Benzhydrocodone Active Metabolite
INFORMATIVE

CYP2D6: Intermediate Metabolizer

The patient's genotype may be associated with reduced conversion of benzhydrocodone to its active metabolite hydromorphone, which may result in decreased effectiveness; however, evidence is insufficient for clinical impact. Benzhydrocodone can be prescribed at standard label-recommended dosage and monitoring. If inadequate analgesic response and opioid use warranted, consider a non-codeine or non-tramadol opioid.

- Crews KR, Monte AA, Huddart R, Caudle KE, Kharasch ED, Gaedigk A, Dunnenberger HM, Leeder JS, Callaghan JT, Samer CF, Klein TE, Haidar CE, Van Driest SL, Ruano G, Sangkuhl K, Cavallari LH, Müller DJ, Prows CA, Nagy M, Somogyi AA, Skaar TC. Clinical Pharmacogenetics Implementation Consortium Guideline for CYP2D6, OPRM1, and COMT Genotypes and Select Opioid Therapy. Clin Pharmacol Ther 2021 10;110(4):888-896.
- Apadaz [package insert]. Newtown, PA: KVK-Tech, Inc.; 2021.

Bupropion
Wellbutrin®, Zyban®, Aplenzin®, Contrave®

Decreased Response to Bupropion for Smoking Cessation
INFORMATIVE

ANKK1: Altered DRD2 function

Smoking Cessation: The patient's genotype result is associated with a positive response to nicotine replacement therapy and a lesser response to bupropion treatment.

- David SP, Strong DR, Munafò MR, Brown RA, Lloyd-Richardson EE, Wileyto PE, Evins AE, Shields PG, Lerman C, Niaura R. Bupropion efficacy for smoking cessation is influenced by the DRD2 Taq1A polymorphism: analysis of pooled data from two clinical trials. Nicotine Tob Res 2007 12;9(12):1251-7.

Citalopram
Celexa®

Increased Citalopram Exposure
ACTIONABLE

CYP2C19: Intermediate Metabolizer

The patient's genotype is associated with an increased exposure to citalopram and may increase risk of adverse effects. Citalopram can be initiated at standard label-recommended dosage. Consider slow up-titration and lower than standard maintenance doses.

- Bousman CA, Stevenson JM, Ramsey LB, Sangkuhl K, Hicks JK, Strawn JR, Singh AB, Ruaño G, Mueller DJ, Tsermpini EE, Brown JT, Bell GC, Leeder JS, Gaedigk A, Scott SA, Klein TE, Caudle KE, Bishop JR. Clinical Pharmacogenetics Implementation Consortium (CPIC) Guideline for CYP2D6, CYP2C19, CYP2B6, SLC6A4, and HTR2A Genotypes and Serotonin Reuptake Inhibitor Antidepressants. Clin Pharmacol Ther. 2023 Apr 9. doi: 10.1002/cpt.2903. Epub ahead of print. PMID: 37032427.

Clomipramine
Anafranil®

Increased Clomipramine Exposure
INFORMATIVE

CYP2D6: Intermediate Metabolizer

The patient is predicted to be a CYP2D6 intermediate metabolizer which is likely to result in decreased metabolism of clomipramine to less active compounds and a subsequent increase in clomipramine exposure leading to side effects.

Psychiatric Conditions: Consider a 25% reduction of the recommended dose and use therapeutic drug monitoring to guide dose adjustments.

- Hicks JK, Sangkuhl K, Swen JJ, Ellingrod VL, Müller DJ, Shimoda K, Bishop JR, Kharasch ED, Skaar TC, Gaedigk A, Dunnenberger HM, Klein TE, Caudle KE, Stingl JC. Clinical pharmacogenetics implementation consortium guideline (CPIC) for CYP2D6 and CYP2C19 genotypes and dosing of tricyclic antidepressants: 2016 update. Clin Pharmacol Ther 2017 07;102(1):37-44.

Increased Clomipramine Exposure
INFORMATIVE

CYP2D6: Intermediate Metabolizer

CYP2C19: Intermediate Metabolizer

The patient's reduced CYP2D6 activity is likely to result in decreased metabolism of clomipramine to less active compounds and a subsequent increase in clomipramine exposure leading to side effects.

Psychiatric Conditions: Consider a 25% reduction of the recommended dose and use therapeutic drug monitoring to guide dose adjustments.

- Hicks JK, Sangkuhl K, Swen JJ, Ellingrod VL, Müller DJ, Shimoda K, Bishop JR, Kharasch ED, Skaar TC, Gaedigk A, Dunnenberger HM, Klein TE, Caudle KE, Stingl JC. Clinical pharmacogenetics implementation consortium guideline (CPIC) for CYP2D6 and CYP2C19 genotypes and dosing of tricyclic antidepressants: 2016 update. Clin Pharmacol Ther 2017 07;102(1):37-44.

Clozapine
Clozaril®

Non-Response to Clozapine
INFORMATIVE

CYP1A2: Normal Metabolizer - Higher Inducibility

Smokers have a high risk for non-response at standard doses and may require higher doses. There is an association between high clozapine doses and the risk of seizures, and therefore careful monitoring is recommended during dosing adjustment. Smoking cessation will increase plasma drug levels, leading to adverse events. Therefore, therapeutic drug monitoring accompanied by dose reduction is recommended in patients who have quit smoking.

- Bolla E, Bortolaso P, Ferrari M, Poloni N, Callegari C, Marino F, Lecchini S, Vender S, Cosentino M. Are CYP1A2*1F and *1C associated with clozapine tolerability?: a preliminary investigation. Psychiatry Res 2011 Oct;189(3):483.
- Ferrari M, Bolla E, Bortolaso P, Callegari C, Poloni N, Lecchini S, Vender S, Marino F, Cosentino M. Association between CYP1A2 polymorphisms and clozapine-induced adverse reactions in patients with schizophrenia. Psychiatry Res 2012 Dec;200(2-3):1014-7.
- Ozdemir V, Kalow W, Okey AB, Lam MS, Albers LJ, Reist C, Fourie J, Posner P, Collins EJ, Roy R. Treatment-resistance to clozapine in association with ultrarapid CYP1A2 activity and the C-->A polymorphism in intron 1 of the CYP1A2 gene: effect of grapefruit juice and low-dose fluvoxamine. J Clin Psychopharmacol 2001 Dec; 21(6):603-7.
- Koonrungsesomboon N, Khatsri R, Wongchompoo P, Teekachunhatean S. The impact of genetic polymorphisms on CYP1A2 activity in humans: a systematic review and meta-analysis. Pharmacogenomics J 2018 12;18(6):760-768.

Unfavorable Response to Clozapine
INFORMATIVE

HTR2A: Homozygous for the C allele (rs6311)

The patient does not carry the HTR2A variant rs6311. Preliminary studies suggest that this genotype may be associated with an unfavorable response to clozapine in patients with European ancestry.

- Arranz MJ, Munro J, Sham P, Kirov G, Murray RM, Collier DA, Kerwin RW. Meta-analysis of studies on genetic variation in 5-HT2A receptors and clozapine response. Schizophr Res 1998 Jul;32(2):93-9.
- Melkersson KI, Gunes A, Dahl ML. Impact of serotonin receptor 2A gene haplotypes on C-peptide levels in clozapine- and olanzapine-treated patients. Hum Psychopharmacol ;25(4):347-52.

Codeine
Codeine; Fioricet® with Codeine

Decreased Exposure to Codeine Active Metabolite
ACTIONABLE

CYP2D6: Intermediate Metabolizer

The patient genotype is associated with decreased conversion of codeine to its active metabolite (morphine), which may result in decreased effectiveness.

Codeine can be prescribed at standard label-recommended age- or weight-based dosing. If no response and opioid use is warranted, consider a non-tramadol opioid. Alternative opioids may include: fentanyl, morphine, hydromorphone, oxymorphone, and tapentadol.

- Crews KR, Monte AA, Huddart R, Caudle KE, Kharasch ED, Gaedigk A, Dunnenberger HM, Leeder JS, Callaghan JT, Samer CF, Klein TE, Haidar CE, Van Driest SL, Ruano G, Sangkuhl K, Cavallari LH, Müller DJ, Prows CA, Nagy M, Somogyi AA, Skaar TC. Clinical Pharmacogenetics Implementation Consortium Guideline for CYP2D6, OPRM1, and COMT Genotypes and Select Opioid Therapy. Clin Pharmacol Ther 2021 10;110(4):888-896.

Desipramine
Norpramin®

Increased Desipramine Exposure
INFORMATIVE

CYP2D6: Intermediate Metabolizer

The patient is predicted to be a CYP2D6 intermediate metabolizer which is likely to result in decreased metabolism of desipramine to less active compounds and a subsequent increase in desipramine exposure leading to side effects.

Psychiatric Conditions: Consider a 25% reduction of the recommended dose and use therapeutic drug monitoring to guide dose adjustments.

- Hicks JK, Sangkuhl K, Swen JJ, Ellingrod VL, Müller DJ, Shimoda K, Bishop JR, Kharasch ED, Skaar TC, Gaedigk A, Dunnenberger HM, Klein TE, Caudle KE, Stingl JC. Clinical pharmacogenetics implementation consortium guideline (CPIC) for CYP2D6 and CYP2C19 genotypes and dosing of tricyclic antidepressants: 2016 update. Clin Pharmacol Ther 2017 07;102(1):37-44.

Dexmethylphenidate
Focalin®

Decreased Response to Dexmethylphenidate
INFORMATIVE

COMT: Intermediate COMT Activity

The patient's genotype result predicts a less optimal response to dexmethylphenidate. Dosage should be individualized according to the needs and response of the patient. Therapy should be initiated in small doses, with gradual weekly increments.

- Cheon KA, Jun JY, Cho DY. Association of the catechol-O-methyltransferase polymorphism with methylphenidate response in a classroom setting in children with attention-deficit hyperactivity disorder. Int Clin Psychopharmacol 2008 Sep;23(5):291-8.
- Kereszturi E, Tarnok Z, Bognar E, Lakatos K, Farkas L, Gadoros J, Sasvari-Szekely M, Nemoda Z. Catechol-O-methyltransferase Val158Met polymorphism is associated with methylphenidate response in ADHD children. Am J Med Genet B Neuropsychiatr Genet 2008 Dec;147B(8):1431-5.

Doxepin
Silenor®

Increased Doxepin Exposure
INFORMATIVE

CYP2D6: Intermediate Metabolizer

The patient is predicted to be a CYP2D6 intermediate metabolizer which is likely to result in decreased metabolism of doxepin to less active compounds and a subsequent increase in doxepin exposure leading to side effects.

Psychiatric Conditions: Consider a 25% reduction of the recommended dose and use therapeutic drug monitoring to guide dose adjustments.

Insomnia: Doxepin can be prescribed according to the standard recommended dosage and administration.

- Hicks JK, Sangkuhl K, Swen JJ, Ellingrod VL, Müller DJ, Shimoda K, Bishop JR, Kharasch ED, Skaar TC, Gaedigk A, Dunnenberger HM, Klein TE, Caudle KE, Stingl JC. Clinical pharmacogenetics implementation consortium guideline (CPIC) for CYP2D6 and CYP2C19 genotypes and dosing of tricyclic antidepressants: 2016 update. Clin Pharmacol Ther 2017 07;102(1):37-44.

Increased Doxepin Exposure
INFORMATIVE

CYP2D6: Intermediate Metabolizer

CYP2C19: Intermediate Metabolizer

The patient's reduced CYP2D6 activity is likely to result in decreased metabolism of doxepin to less active compounds and a subsequent increase in doxepin exposure leading to side effects.

Psychiatric Conditions: Consider a 25% reduction of the recommended dose and use therapeutic drug monitoring to guide dose adjustments.

Insomnia: Doxepin can be prescribed according to the standard recommended dosage and administration.

- Hicks JK, Sangkuhl K, Swen JJ, Ellingrod VL, Müller DJ, Shimoda K, Bishop JR, Kharasch ED, Skaar TC, Gaedigk A, Dunnenberger HM, Klein TE, Caudle KE, Stingl JC. Clinical pharmacogenetics implementation consortium guideline (CPIC) for CYP2D6 and CYP2C19 genotypes and dosing of tricyclic antidepressants: 2016 update. Clin Pharmacol Ther 2017 07;102(1):37-44.

PRECISION GENETICS

Sample Org
123 Street Street Greenville, SC 29615

PATIENT INFORMATION	
NAME:	test14 test14
DOB:	04/29/1962
SEX:	Female

SPECIMEN DETAILS	
SAMPLE ID:	PGT-24-001-14
SPECIMEN TYPE:	None
COLLECTION DATE:	02/21/2024
RECEIVED DATE:	02/23/2024
REPORT DATE:	05/16/2024

PROVIDER INFORMATION	
PROVIDER:	LOREN KIDD
FACILITY:	Medical Office

Escitalopram
Lexapro®

Increased Escitalopram Exposure
ACTIONABLE

CYP2C19: Intermediate Metabolizer

The patient's genotype is associated with an increased exposure to escitalopram and may increase risk of adverse effects. Escitalopram can be initiated at standard label-recommended dosage. Consider slow up-titration and lower than standard maintenance doses.

• Bousman CA, Stevenson JM, Ramsey LB, Sangkuhl K, Hicks JK, Strawn JR, Singh AB, Ruaño G, Mueller DJ, Tsermpini EE, Brown JT, Bell GC, Leeder JS, Gaedigk A, Scott SA, Klein TE, Caudle KE, Bishop JR. Clinical Pharmacogenetics Implementation Consortium (CPIC) Guideline for CYP2D6, CYP2C19, CYP2B6, SLC6A4, and HTR2A Genotypes and Serotonin Reuptake Inhibitor Antidepressants. Clin Pharmacol Ther. 2023 Apr 9. doi: 10.1002/cpt.2903. Epub ahead of print. PMID: 37032427.

Flecainide
Tambocor®

Increased Exposure to Flecainide
ACTIONABLE

CYP2D6: Intermediate Metabolizer

The patient's genotype may be associated with an increased flecainide exposure following standard dosing. Consider prescribing a lower flecainide dose for therapeutic indications. When compared to a CYP2D6 normal metabolizer, an intermediate metabolizer may require a 25% dose reduction. Careful titration with ECG recording and monitoring of flecainide plasma concentrations are recommended until a favorable clinical response is achieved.

Dose adjustments are not required when flecainide is utilized for diagnostic uses.

• The Royal Dutch Pharmacists Association of the KNMP. (2020). Pharmacogenetic Recommendations 2020 [PDF file]. Retrieved from https://www.knmp.nl/downloads/pharmacogenetic-recommendations-august-2020.pdf (Accessed September 8, 2020).

Fluvoxamine
Luvox®

Increased Fluvoxamine Exposure
ACTIONABLE

CYP2D6: Intermediate Metabolizer

The patient's genotype is associated with an increased exposure to fluvoxamine, which may increase risk of adverse effects. Fluvoxamine can be prescribed at standard label-recommended dosage with close monitoring.

• Bousman CA, Stevenson JM, Ramsey LB, Sangkuhl K, Hicks JK, Strawn JR, Singh AB, Ruaño G, Mueller DJ, Tsermpini EE, Brown JT, Bell GC, Leeder JS, Gaedigk A, Scott SA, Klein TE, Caudle KE, Bishop JR. Clinical Pharmacogenetics Implementation Consortium (CPIC) Guideline for CYP2D6, CYP2C19, CYP2B6, SLC6A4, and HTR2A Genotypes and Serotonin Reuptake Inhibitor Antidepressants. Clin Pharmacol Ther. 2023 Apr 9. doi: 10.1002/cpt.2903. Epub ahead of print. PMID: 37032427.

Granisetron
Sancuso®, Sustol®

Unfavorable Response to Standard Granisetron Dosing
INFORMATIVE

ABCB1: Variant Allele Not Present

The genotype result predicts that the patient has decreased ABCB1 transporter expression. Patients with this genotype may experience decreased efficacy. No dose adjustments are recommended.

• Babaoglu MO, Bayar B, Aynacioglu AS, Kerb R, Abali H, Celik I, Bozkurt A. Association of the ABCB1 3435C>T polymorphism with antiemetic efficacy of 5-hydroxytryptamine type 3 antagonists. Clin Pharmacol Ther 2005 Dec;78(6):619-26.

Hydrocodone
Vicodin®

Possible Decreased Exposure to Hydrocodone Active Metabolite
INFORMATIVE

CYP2D6: Intermediate Metabolizer

The patient genotype may be associated with a reduced conversion of hydrocodone to an active metabolite (hydromorphone), which may result in decreased effectiveness.

Hydrocodone can be prescribed at standard label-recommended age- or weight-based dosing. If no response and opioid use is warranted, consider a non-codeine or non-tramadol opioid. Alternative opioids may include: fentanyl, morphine, hydromorphone, oxymorphone, and tapentadol.

• Crews KR, Monte AA, Huddart R, Caudle KE, Kharasch ED, Gaedigk A, Dunnenberger HM, Leeder JS, Callaghan JT, Samer CF, Klein TE, Haidar CE, Van Driest SL, Ruano G, Sangkuhl K, Cavallari LH, Müller DJ, Prows CA, Nagy M, Somogyi AA, Skaar TC. Clinical Pharmacogenetics Implementation Consortium Guideline for CYP2D6, OPRM1, and COMT Genotypes and Select Opioid Therapy. Clin Pharmacol Ther 2021 10;110(4):888-896.

PRECISION GENETICS

Sample Org
123 Street Street Greenville, SC 29615

PATIENT INFORMATION	
NAME:	test14 test14
DOB:	04/29/1962
SEX:	Female

SPECIMEN DETAILS	
SAMPLE ID:	PGT-24-001-14
SPECIMEN TYPE:	None
COLLECTION DATE:	02/21/2024
RECEIVED DATE:	02/23/2024
REPORT DATE:	05/16/2024

PROVIDER INFORMATION	
PROVIDER:	LOREN KIDD
FACILITY:	Medical Office

Iloperidone
Fanapt®

Moderate Sensitivity to Iloperidone
ACTIONABLE

CYP2D6: Intermediate Metabolizer

Because iloperidone is associated with QTc prolongation, caution is warranted when prescribing the drug in patients with reduced CYP2D6 activity. Iloperidone must be titrated slowly from a low starting dose to avoid orthostatic hypotension. If patients taking iloperidone experience symptoms that could indicate the occurrence of cardiac arrhythmias (e.g., dizziness, palpitations, or syncope), the prescriber should initiate further evaluation, including cardiac monitoring.

- Fanapt [package insert]. East Hanover, NJ: Novartis Pharmaceuticals Corporation; 2012.

Imipramine
Tofranil®

Increased Imipramine Exposure
INFORMATIVE

CYP2D6: Intermediate Metabolizer

The patient is predicted to be a CYP2D6 intermediate metabolizer which is likely to result in decreased metabolism of imipramine to less active compounds and a subsequent increase in imipramine exposure leading to side effects.

Psychiatric Conditions: Consider a 25% reduction of the recommended dose and use therapeutic drug monitoring to guide dose adjustments.

- Hicks JK, Sangkuhl K, Swen JJ, Ellingrod VL, Müller DJ, Shimoda K, Bishop JR, Kharasch ED, Skaar TC, Gaedigk A, Dunnenberger HM, Klein TE, Caudle KE, Stingl JC. Clinical pharmacogenetics implementation consortium guideline (CPIC) for CYP2D6 and CYP2C19 genotypes and dosing of tricyclic antidepressants: 2016 update. Clin Pharmacol Ther 2017 07;102(1):37-44.

Increased Imipramine Exposure
INFORMATIVE

CYP2D6: Intermediate Metabolizer

CYP2C19: Intermediate Metabolizer

The patient's reduced CYP2D6 activity is likely to result in decreased metabolism of imipramine to less active compounds and a subsequent increase in imipramine exposure leading to side effects.

Psychiatric Conditions: Consider a 25% reduction of the recommended dose and use therapeutic drug monitoring to guide dose adjustments.

- Hicks JK, Sangkuhl K, Swen JJ, Ellingrod VL, Müller DJ, Shimoda K, Bishop JR, Kharasch ED, Skaar TC, Gaedigk A, Dunnenberger HM, Klein TE, Caudle KE, Stingl JC. Clinical pharmacogenetics implementation consortium guideline (CPIC) for CYP2D6 and CYP2C19 genotypes and dosing of tricyclic antidepressants: 2016 update. Clin Pharmacol Ther 2017 07;102(1):37-44.

Leflunomide
Arava®

Increased Exposure to Leflunomide
INFORMATIVE

CYP2C19: Intermediate Metabolizer

Leflunomide is metabolized by CYP2C19 and CYP1A2 to its active metabolite teriflunomide. Preliminary studies indicate that patients with decreased CYP2C19 activity have a higher risk of developing gastrointestinal side effects and hepatotoxicity. There is insufficient data to calculate dose adjustment. If leflunomide is prescribed at standard dosing, monitor closely the patient's response and be alert to increased side effects.

Full blood cell count (CBC) and liver function parameters should be checked no more than 6 months before beginning treatment, and every month for the initial 6 months of therapy. Blood pressure should be checked before beginning treatment and periodically thereafter.

- Wiese MD, Schnabl M, O'Doherty C, Spargo LD, Sorich MJ, Cleland LG, Proudman SM. Polymorphisms in cytochrome P450 2C19 enzyme and cessation of leflunomide in patients with rheumatoid arthritis. Arthritis Res Ther 2012 Jul;14(4):R163.
- Bohanec Grabar P, Grabnar I, Rozman B, Logar D, Tomsic M, Suput D, Trdan T, Peterlin Masic L, Mrhar A, Dolzan V. Investigation of the influence of CYP1A2 and CYP2C19 genetic polymorphism on 2-Cyano-3-hydroxy-N-[4-(trifluoromethyl)phenyl]-2-butenamide (A77 1726) pharmacokinetics in leflunomide-treated patients with rheumatoid arthritis. Drug Metab Dispos 2009 Oct;37(10):2061-8.

Lorazepam
Ativan®

Possible Altered Response to Lorazepam
INFORMATIVE

UGT2B15: Poor Function

Lorazepam clearance is reduced in this patient. However, there is insufficient evidence whether this change results in a significant clinical effect. Consider monitoring the patient for increased sedation and adjust dosing accordingly.

- Chung JY, Cho JY, Yu KS, Kim JR, Jung HR, Lim KS, Jang IJ, Shin SG. Effect of the UGT2B15 genotype on the pharmacokinetics, pharmacodynamics, and drug interactions of intravenous lorazepam in healthy volunteers. Clin Pharmacol Ther 2005 Jun;77(6):486-94.

Maprotiline
Ludiomil®

Possible Increased Maprotiline Exposure
INFORMATIVE

CYP2D6: Intermediate Metabolizer

Like other tricyclic and tetracyclic antidepressants, maprotiline is metabolized by CYP2D6 as well as CYP1A2. Decreased CYP2D6 activity results in higher maprotiline concentrations potentially leading to higher adverse events. There are no established dosing adjustments for patients with decreased CYP2D6 function therefore, therapy must be initiated at a low dosage and gradually adjusted according to the patient's response. The lowest effective dosage should always be considered during maintenance therapy.

- Firkusny L, Gleiter CH. Maprotiline metabolism appears to co-segregate with the genetically-determined CYP2D6 polymorphic hydroxylation of debrisoquine. Br J Clin Pharmacol 1994 Apr;37(4):383-8.
- Maprotyline Hydrochloride [package insert]. Morgantown, WV: Mylan Pharmaceuticals Inc.; 2014.

Mavacamten
Camzyos®

Increased Mavacamten Exposure
ACTIONABLE

CYP2C19: Intermediate Metabolizer

The genotype result indicates increased exposure to mavacamten and a possible increased risk of adverse effects including heart failure. Dosages are titrated to individual response and CYP2C19 genetic variation is accounted for in FDA dose titration and monitoring schedules. Mavacamten can be prescribed at standard label-recommended dosage and monitoring.

- Camzyos [package insert]. Princeton, NJ: Bristol-Myers Squibb Company; 2022.

Meclizine
Antivert®

Increased Exposure to Meclizine
ACTIONABLE

CYP2D6: Intermediate Metabolizer

Genetic polymorphism of CYP2D6 could contribute to large inter-individual variability in meclizine exposure. Meclizine can be prescribed at standard label-recommended dosage and administration. Consider increased monitoring for adverse effects.

- FDA Table of Pharmacogenetic Associations
- Antivert [package insert]. East Brunswick, NJ: Casper Pharma LLC; 2019.

Mercaptopurine
Purinethol®, Purixan®

Increased Risk of Myelotoxicity
ACTIONABLE

TPMT: Poor or Intermediate Metabolizer

NUDT15: Normal Metabolizer

The TPMT genotype results for this patient are indicative of a *1/*3A predicting intermediate TPMT activity. However, there is a small risk (<1 in 100,000) that this patient's genotype is instead *3B/*3C which would predict a low TPMT activity. A TPMT phenotype test could distinguish between these possible phenotypes.

Evidence shows that 30 to 60% of patients with these genotype results experience severe leukopenia, neutropenia or myelosuppression with standard doses of mercaptopurine.

Nonmalignant indications

Therapy initiation: if normal starting dose is 1.5mg/kg/day, consider decreasing start dose to 30-80% of normal dose and adjust subsequent doses based on disease-specific guidelines and/or myelosuppression, as needed. Allow 2-4 weeks to reach steady state after each dose adjustment. A dose reduction may not be needed when the initiation dose considered is below 1.5mg/kg/day. Alternative medications may also be considered.

Malignant indications

Therapy initiation: if normal starting dose is 75mg/m^2/day (1.5mg/kg/day), consider decreasing start dose to 30-80% of normal dose and adjust subsequent doses based on disease-specific guidelines and myelosuppression. Allow 2-4 weeks to reach steady state after each dose adjustment.

These genotype results cannot be used to assess the patient's risk of thiopurine-related pancreatitis or hepatotoxicity.

- Relling MV, Schwab M, Whirl-Carrillo M, Suarez-Kurtz G, Pui CH, Stein CM, Moyer AM, Evans WE, Klein TE, Antillon-Klussmann FG, Caudle KE, Kato M, Yeoh AEJ, Schmiegelow K, Yang JJ. Clinical Pharmacogenetics Implementation Consortium Guideline for Thiopurine Dosing Based on TPMT and NUDT15 Genotypes: 2018 Update. Clin Pharmacol Ther 2019 May;105(5):1095-1105.

PRECISION GENETICS

Sample Org
123 Street Street Greenville, SC 29615

PATIENT INFORMATION	
NAME:	test14 test14
DOB:	04/29/1962
SEX:	Female

SPECIMEN DETAILS	
SAMPLE ID:	PGT-24-001-14
SPECIMEN TYPE:	None
COLLECTION DATE:	02/21/2024
RECEIVED DATE:	02/23/2024
REPORT DATE:	05/16/2024

PROVIDER INFORMATION	
PROVIDER:	LOREN KIDD
FACILITY:	Medical Office

Methylphenidate
Ritalin®, Aptensio XR®, Concerta®, Metadate ER®, Quillivant ER®

Decreased Response to Methylphenidate
INFORMATIVE

COMT: Intermediate COMT Activity

The patient's genotype result predicts a less optimal response to methylphenidate. Dosage should be individualized according to the needs and response of the patient. Therapy should be initiated in small doses, with gradual weekly increments.

- Cheon KA, Jun JY, Cho DY. Association of the catechol-O-methyltransferase polymorphism with methylphenidate response in a classroom setting in children with attention-deficit hyperactivity disorder. Int Clin Psychopharmacol 2008 Sep;23(5):291-8.

Metoclopramide
Reglan®

Possible Sensitivity to Metoclopramide
INFORMATIVE

CYP2D6: Intermediate Metabolizer

There is no data documenting the changes in plasma concentrations of metoclopramide in CYP2D6 intermediate metabolizers. Metoclopramide can be prescribed at standard label-recommended dosage and administration with careful monitoring for possible increase of side effects.

- Reglan [package insert]. Baudette, MN: ANI Pharmaceuticals, Inc.; 2017.

Metoprolol
Lopressor®

Increased Exposure to Metoprolol
ACTIONABLE

CYP2D6: Intermediate Metabolizer

The patient's genotype may be associated with an increased metoprolol exposure following standard dosing. When compared to a normal metabolizer, an intermediate metabolizer may require a 50% dose reduction. If metoprolol is prescribed, be alert to adverse events (e.g., bradycardia or cold extremities).

- The Royal Dutch Pharmacists Association of the KNMP. (2020). Pharmacogenetic Recommendations 2020 [PDF file]. Retrieved from https://www.knmp.nl/downloads/pharmacogenetic-recommendations-august-2020.pdf (Accessed September 8, 2020).

Mexiletine
Mexitil®

Increased Sensitivity to Mexiletine
ACTIONABLE

CYP2D6: Intermediate Metabolizer

Consider prescribing a lower mexiletine dose. A slow titration with ECG recording and monitoring of mexiletine plasma concentrations are recommended until a favorable clinical response is achieved.

- MEXILETINE HYDROCHLORIDE- mexiletine hydrochloride capsule [package insert]. Sellersville, PA: Teva Pharmaceuticals USA. https://dailymed.nlm.nih.gov/dailymed/getFile.cfm?setid=ca648488-4f8d-4d26-be4d-6a75fbb8b62c&type=pdf&name=ca648488-4f8d-4d26-be4d-6a75fbb8b62c. Rev Apr 2012.
- Otani M, Fukuda T, Naohara M, Maune H, Senda C, Yamamoto I, Azuma J. Impact of CYP2D6*10 on mexiletine pharmacokinetics in healthy adult volunteers. Eur J Clin Pharmacol 2003 Sep;59(5-6):395-9.
- Hanioka N, Okumura Y, Saito Y, Hichiya H, Soyama A, Saito K, Ueno K, Sawada J, Narimatsu S. Catalytic roles of CYP2D6.10 and CYP2D6.36 enzymes in mexiletine metabolism: in vitro functional analysis of recombinant proteins expressed in Saccharomyces cerevisiae. Biochem Pharmacol 2006 Apr;71(9):1386-95.

Naltrexone
Vivitrol®, Contrave®

Altered Response to Naltrexone
INFORMATIVE

OPRM1: Normal OPRM1 Function

Treatment of alcohol dependence: the patient has the OPRM1 118AA wild-type genotype that is associated with a poorer outcome with naltrexone therapy. Naltrexone-treated patients not carrying the OPRM1 118A>G G allele are less likely to respond to this drug, and may have higher relapse rates than those who are carriers of this allele. This association has not been reported consistently across studies.

- Kranzler HR, Armeli S, Covault J, Tennen H. Variation in OPRM1 moderates the effect of desire to drink on subsequent drinking and its attenuation by naltrexone treatment. Addict Biol 2013 Jan;18(1):193-201.
- Chamorro AJ, Marcos M, Mirón-Canelo JA, Pastor I, González-Sarmiento R, Laso FJ. Association of μ-opioid receptor (OPRM1) gene polymorphism with response to naltrexone in alcohol dependence: a systematic review and meta-analysis. Addict Biol 2012 May;17(3):505-12.
- Coller JK, Cahill S, Edmonds C, Farquharson AL, Longo M, Minniti R, Sullivan T, Somogyi AA, White JM. OPRM1 A118G genotype fails to predict the effectiveness of naltrexone treatment for alcohol dependence. Pharmacogenet Genomics 2011 Dec;21(12):902-5.

Sample Org
123 Street Street Greenville, SC 29615

PATIENT INFORMATION		SPECIMEN DETAILS		PROVIDER INFORMATION	
NAME:	test14 test14	SAMPLE ID:	PGT-24-001-14	PROVIDER:	LOREN KIDD
DOB:	04/29/1962	SPECIMEN TYPE:	None	FACILITY:	Medical Office
SEX:	Female	COLLECTION DATE:	02/21/2024		
		RECEIVED DATE:	02/23/2024		
		REPORT DATE:	05/16/2024		

Nortriptyline
Pamelor®

Increased Nortriptyline Exposure
ACTIONABLE

CYP2D6: Intermediate Metabolizer

The patient is predicted to be a CYP2D6 intermediate metabolizer which is likely to result in decreased metabolism of nortriptyline to less active compounds and a subsequent increase in nortriptyline exposure leading to side effects.

Psychiatric Conditions: Consider a 25% reduction of the recommended dose and use therapeutic drug monitoring to guide dose adjustments.

- Hicks JK, Sangkuhl K, Swen JJ, Ellingrod VL, Müller DJ, Shimoda K, Bishop JR, Kharasch ED, Skaar TC, Gaedigk A, Dunnenberger HM, Klein TE, Caudle KE, Stingl JC. Clinical pharmacogenetics implementation consortium guideline (CPIC) for CYP2D6 and CYP2C19 genotypes and dosing of tricyclic antidepressants: 2016 update. Clin Pharmacol Ther 2017 07;102(1):37-44.

Olanzapine
Zyprexa®

Non-Response to Olanzapine
INFORMATIVE

CYP1A2: Normal Metabolizer - Higher Inducibility

There is little evidence regarding the impact of CYP1A2 genetic variants on olanzapine response. Smokers may be at risk for non-response at standard doses. Careful monitoring is recommended during dosing adjustment. Smoking cessation may increase plasma drug levels, leading to adverse events. Therefore, therapeutic drug monitoring accompanied by dose reduction may be needed in patients who have quit smoking.

- Perera V, Gross AS, Polasek TM, Qin Y, Rao G, Forrest A, Xu J, McLachlan AJ. Considering CYP1A2 phenotype and genotype for optimizing the dose of olanzapine in the management of schizophrenia. Expert Opin Drug Metab Toxicol 2013 Sep;9(9):1115-37.
- Laika B, Leucht S, Heres S, Schneider H, Steimer W. Pharmacogenetics and olanzapine treatment: CYP1A2*1F and serotonergic polymorphisms influence therapeutic outcome. Pharmacogenomics J 2010 Feb;10(1):20-9.
- Koonrungsesomboon N, Khatsri R, Wongchompoo P, Teekachunhatean S. The impact of genetic polymorphisms on CYP1A2 activity in humans: a systematic review and meta-analysis. Pharmacogenomics J 2018 12;18(6):760-768.

Ondansetron
Zofran®, Zuplenz®

Unfavorable Response to Standard Ondansetron Dosing
INFORMATIVE

ABCB1: Variant Allele Not Present

The genotype result predicts that the patient has decreased ABCB1 transporter expression. Patients with this genotype may experience decreased efficacy. No dose adjustments are recommended.

- Perwitasari DA, Wessels JA, van der Straaten RJ, Baak-Pablo RF, Mustofa M, Hakimi M, Nortier JW, Gelderblom H, Guchelaar HJ. Association of ABCB1, 5-HT3B receptor and CYP2D6 genetic polymorphisms with ondansetron and metoclopramide antiemetic response in Indonesian cancer patients treated with highly emetogenic chemotherapy. Jpn J Clin Oncol 2011 Oct;41(10):1168-76.
- Babaoglu MO, Bayar B, Aynacioglu AS, Kerb R, Abali H, Celik I, Bozkurt A. Association of the ABCB1 3435C>T polymorphism with antiemetic efficacy of 5-hydroxytryptamine type 3 antagonists. Clin Pharmacol Ther 2005 Dec;78(6):619-26.

Oxazepam
Serax®

Possible Altered Response to Oxazepam
INFORMATIVE

UGT2B15: Poor Function

Oxazepam clearance is reduced in this patient. However, there is insufficient evidence whether this change results in a significant clinical effect. Consider monitoring the patient for increased sedation and adjust dosing accordingly.

- He X, Hesse LM, Hazarika S, Masse G, Harmatz JS, Greenblatt DJ, Court MH. Evidence for oxazepam as an in vivo probe of UGT2B15: oxazepam clearance is reduced by UGT2B15 D85Y polymorphism but unaffected by UGT2B17 deletion. Br J Clin Pharmacol 2009 Nov;68(5):721-30.
- Court MH, Hao Q, Krishnaswamy S, Bekaii-Saab T, Al-Rohaimi A, von Moltke LL, Greenblatt DJ. UDP-glucuronosyltransferase (UGT) 2B15 pharmacogenetics: UGT2B15 D85Y genotype and gender are major determinants of oxazepam glucuronidation by human liver. J Pharmacol Exp Ther 2004 Aug;310(2):656-65.
- Court MH, Duan SX, Guillemette C, Journault K, Krishnaswamy S, Von Moltke LL, Greenblatt DJ. Stereoselective conjugation of oxazepam by human UDP-glucuronosyltransferases (UGTs): S-oxazepam is glucuronidated by UGT2B15, while R-oxazepam is glucuronidated by UGT2B7 and UGT1A9. Drug Metab Dispos 2002 Nov;30(11):1257-65.

Paroxetine
Paxil®, Brisdelle®

Increased Paroxetine Exposure
INFORMATIVE

CYP2D6: Intermediate Metabolizer

The patient's genotype is associated with an increased exposure to paroxetine when starting treatment or at lower doses, which may increase risk of adverse effects. Consider prescribing paroxetine at a lower starting dose and slower up-titration with close monitoring.

- Bousman CA, Stevenson JM, Ramsey LB, Sangkuhl K, Hicks JK, Strawn JR, Singh AB, Ruaño G, Mueller DJ, Tsermpini EE, Brown JT, Bell GC, Leeder JS, Gaedigk A, Scott SA, Klein TE, Caudle KE, Bishop JR. Clinical Pharmacogenetics Implementation Consortium (CPIC) Guideline for CYP2D6, CYP2C19, CYP2B6, SLC6A4, and HTR2A Genotypes and Serotonin Reuptake Inhibitor Antidepressants. Clin Pharmacol Ther. 2023 Apr 9. doi: 10.1002/cpt.2903. Epub ahead of print. PMID: 37032427.

PRECISION GENETICS

Sample Org
123 Street Street Greenville, SC 29615

PATIENT INFORMATION	
NAME:	test14 test14
DOB:	04/29/1962
SEX:	Female

SPECIMEN DETAILS	
SAMPLE ID:	PGT-24-001-14
SPECIMEN TYPE:	None
COLLECTION DATE:	02/21/2024
RECEIVED DATE:	02/23/2024
REPORT DATE:	05/16/2024

PROVIDER INFORMATION	
PROVIDER:	LOREN KIDD
FACILITY:	Medical Office

Perphenazine
Trilafon®

Possible Sensitivity to Perphenazine
ACTIONABLE

CYP2D6: Intermediate Metabolizer

Patients with a decreased CYP2D6 function will eliminate perphenazine more slowly, which can result in higher drug concentrations and possibly more adverse events (extrapyramidal symptoms). Consider close monitoring and dose reduction to avoid toxicity.

- Jerling M, Dahl ML, Aberg-Wistedt A, Liljenberg B, Landell NE, Bertilsson L, Sjöqvist F. The CYP2D6 genotype predicts the oral clearance of the neuroleptic agents perphenazine and zuclopenthixol. Clin Pharmacol Ther 1996 Apr;59(4):423-8.
- Dahl-Puustinen ML, Lidén A, Alm C, Nordin C, Bertilsson L. Disposition of perphenazine is related to polymorphic debrisoquin hydroxylation in human beings. Clin Pharmacol Ther 1989 Jul;46(1):78-81.
- Pollock BG, Mulsant BH, Sweet RA, Rosen J, Altieri LP, Perel JM. Prospective cytochrome P450 phenotyping for neuroleptic treatment in dementia. Psychopharmacol Bull 1995 ;31(2):327-31.
- Linnet K, Wiborg O. Steady-state serum concentrations of the neuroleptic perphenazine in relation to CYP2D6 genetic polymorphism. Clin Pharmacol Ther 1996 Jul;60(1):41-7.
- Perphenazine [package insert]. Princeton, NJ: Sandoz Inc.; 2010.

Phenobarbital
Luminal®

Possible Sensitivity to Phenobarbital
INFORMATIVE

CYP2C19: Intermediate Metabolizer

CYP2C19 is partly involved in the metabolism of phenobarbital, and although CYP2C19 intermediate metabolizers have a lower clearance of phenobarbital than normal metabolizers, no significant changes in clinical outcome has been reported with this antiepileptic drug. Therefore, phenobarbital can be prescribed at standard label-recommended dosage and administration with a closer monitoring for adverse events.

- Lee SM, Chung JY, Lee YM, Park MS, Namgung R, Park KI, Lee C. Effects of cytochrome P450 (CYP)2C19 polymorphisms on pharmacokinetics of phenobarbital in neonates and infants with seizures. Arch Dis Child 2012 Jun;97(6):569-72.
- Mamiya K, Hadama A, Yukawa E, Ieiri I, Otsubo K, Ninomiya H, Tashiro N, Higuchi S. CYP2C19 polymorphism effect on phenobarbitone. Pharmacokinetics in Japanese patients with epilepsy: analysis by population pharmacokinetics. Eur J Clin Pharmacol ;55(11-12):821-5.
- Yukawa E, Mamiya K. Effect of CYP2C19 genetic polymorphism on pharmacokinetics of phenytoin and phenobarbital in Japanese epileptic patients using Non-linear Mixed Effects Model approach. J Clin Pharm Ther 2006 Jun;31(3):275-82.
- Anderson, Gail D. "Chemisry, Biotransformation, and Pharmacokinetics." Antiepileptic Drugs. 5th ed. Philadelphia: Lippincott Williams & Wilkins, 2002. 496-03. Print.

Primidone
Mysoline®

Possible Sensitivity to Primidone
INFORMATIVE

CYP2C19: Intermediate Metabolizer

CYP2C19 is partly involved in the metabolism of primidone, and although CYP2C19 intermediate metabolizers have a lower clearance of phenobarbital (active metabolite) than normal metabolizers, no significant changes in clinical outcome has been reported with this antiepileptic drug. Therefore, primidone can be prescribed at standard label-recommended dosage and administration with a closer monitoring for adverse events.

- Fincham, Richard W., and Dorothy D. Schottelius. "Primidone." Antiepileptic Drugs. 5th ed. Philadelphia: Lippincott Williams & Wilkins, 2002. 621-36. Print.

Propafenone
Rythmol®

Increased Exposure to Propafenone
ACTIONABLE

CYP2D6: Intermediate Metabolizer

The patient's genotype may be associated with an increased propafenone exposure following standard dosing. There is insufficient data to allow calculation of dose adjustment. Titrate carefully and adjust the dose in response to plasma concentration and ECG monitoring. An alternative medication such as sotalol, disopyramide, quinidine or amiodarone may also be considered.

Dose adjustments with co-medications: concurrent use of propafenone along with CYP3A4 inhibitors and CYP2D6 inhibitors may significantly increase the plasma concentration of propafenone increasing the risk of proarrhythmia and other adverse events. Therefore, avoid simultaneous use of propafenone with both a CYP2D6 inhibitor and a CYP3A4 inhibitor.

- Rythmol [package insert]. Research Triangle Park, NC: GlaxoSmithKline; 2018.
- Rythmol SR [package insert]. Research Triangle Park, NC: GlaxoSmithKline; 2018.
- The Royal Dutch Pharmacists Association of the KNMP. (2020). Pharmacogenetic Recommendations 2020 [PDF file]. Retrieved from https://www.knmp.nl/downloads/pharmacogenetic-recommendations-august-2020.pdf (Accessed September 8, 2020).

Protriptyline
Vivactil®

Possible Increased Protriptyline Exposure
INFORMATIVE

CYP2D6: Intermediate Metabolizer

Like other tricyclic and tetracyclic antidepressants, protriptyline is metabolized by CYP2D6. Decreased CYP2D6 activity results in higher protriptyline concentrations potentially leading to higher adverse events. There are no established dosing adjustments for patients with decreased CYP2D6 function. Therefore, therapy must be initiated at a low dosage and gradually adjusted according to the patient's response. The lowest effective dosage should always be considered during maintenance therapy.

• Vivactil [package insert]. Horsham, PA: Teva Pharmaceuticals USA, Inc.; 2014.

Sertraline
Zoloft®

Increased Sertraline Exposure
ACTIONABLE

CYP2C19: Intermediate Metabolizer

CYP2B6: Normal Metabolizer

The patient's genotype is associated with an increased exposure to sertraline and may increase risk of adverse effects. Sertraline can be initiated at standard label-recommended dosage. Consider slow up-titration and lower than standard label-recommended maintenance doses.

• Bousman CA, Stevenson JM, Ramsey LB, Sangkuhl K, Hicks JK, Strawn JR, Singh AB, Ruaño G, Mueller DJ, Tsermpini EE, Brown JT, Bell GC, Leeder JS, Gaedigk A, Scott SA, Klein TE, Caudle KE, Bishop JR. Clinical Pharmacogenetics Implementation Consortium (CPIC) Guideline for CYP2D6, CYP2C19, CYP2B6, SLC6A4, and HTR2A Genotypes and Serotonin Reuptake Inhibitor Antidepressants. Clin Pharmacol Ther. 2023 Apr 9. doi: 10.1002/cpt.2903. Epub ahead of print. PMID: 37032427.

Sulfasalazine
Azulfidine®, Sulfazine®

Decreased Response to Sulfasalazine For the Treatment of Rheumatoid Arthritis
INFORMATIVE

ABCG2: Normal Function

Rheumatoid Arthritis: The patient carries two copies of ABCG2 rs2231142 C allele. Preliminary data suggests that this genotype may be associated with decreased plasma levels of sulfasalazine which may decrease the likelihood of response to this drug.

• Wiese MD, Alotaibi N, O'Doherty C, Sorich MJ, Suppiah V, Cleland LG, Proudman SM. Pharmacogenomics of NAT2 and ABCG2 influence the toxicity and efficacy of sulphasalazine containing DMARD regimens in early rheumatoid arthritis. Pharmacogenomics J 2014 Aug;14(4):350-5.
• Gotanda K, Tokumoto T, Hirota T, Fukae M, Ieiri I. Sulfasalazine disposition in a subject with 376C>T (nonsense mutation) and 421C>A variants in the ABCG2 gene. Br J Clin Pharmacol 2015 Nov;80(5):1236-7.

Tetrabenazine
Xenazine®

Normal Sensitivity to Tetrabenazine
ACTIONABLE

CYP2D6: Intermediate Metabolizer

For treating chorea associated with Huntington's disease: Individualization of dose with careful weekly titration is required. The first week's starting dose is 12.5 mg daily; second week, 25 mg (12.5 mg twice daily); then slowly titrate at weekly intervals by 12.5 mg to a tolerated dose. **The maximum daily dose in CYP2D6 intermediate metabolizers of CYP2D6 is 100 mg with a maximum single dose of 37.5 mg**. If serious adverse events occur, titration should be stopped and the dose of tetrabenazine should be reduced. If the adverse event(s) do not resolve, consider withdrawal of tetrabenazine.

• Xenazine [package insert]. Deerfield, IL: Lundbeck Inc.; 2017.

Sample Org
123 Street Street Greenville, SC 29615

PATIENT INFORMATION		SPECIMEN DETAILS		PROVIDER INFORMATION	
NAME:	test14 test14	SAMPLE ID:	PGT-24-001-14	PROVIDER:	LOREN KIDD
DOB:	04/29/1962	SPECIMEN TYPE:	None	FACILITY:	Medical Office
SEX:	Female	COLLECTION DATE:	02/21/2024		
		RECEIVED DATE:	02/23/2024		
		REPORT DATE:	05/16/2024		

Thioguanine
Tabloid®

Increased Risk of Myelotoxicity
ACTIONABLE

TPMT: Poor or Intermediate Metabolizer
NUDT15: Normal Metabolizer

The TPMT genotype results for this patient are indicative of a *1/*3A predicting intermediate TPMT activity. However, there is a small risk (<1 in 100,000) that this patient's genotype is instead *3B/*3C which would predict a low TPMT activity. A TPMT phenotype test could distinguish between these possible phenotypes.

Evidence shows that 30 to 60% of patients with these genotype results experience severe leukopenia, neutropenia or myelosuppression with standard doses of thioguanine.

Nonmalignant indications

Therapy initiation: if normal starting dose is ≥ 40-60mg/m^2/day, consider decreasing start dose to 50-80% of normal dose and adjust subsequent doses based on disease-specific guidelines and/or myelosuppression, as needed. Allow 2-4 weeks to reach steady state after each dose adjustment. Alternative medications may also be considered.

Malignant indications

Therapy initiation: if normal starting dose is ≥ 40-60mg/m^2/day, consider decreasing start dose to 50-80% of normal dose and adjust subsequent doses based on disease-specific guidelines and myelosuppression. Allow 2-4 weeks to reach steady state after each dose adjustment.

These genotype results cannot be used to assess the patient's risk of thiopurine-related pancreatitis or hepatotoxicity.

- Relling MV, Schwab M, Whirl-Carrillo M, Suarez-Kurtz G, Pui CH, Stein CM, Moyer AM, Evans WE, Klein TE, Antillon-Klussmann FG, Caudle KE, Kato M, Yeoh AEJ, Schmiegelow K, Yang JJ. Clinical Pharmacogenetics Implementation Consortium Guideline for Thiopurine Dosing Based on TPMT and NUDT15 Genotypes: 2018 Update. Clin Pharmacol Ther 2019 May;105(5):1095-1105.

Timolol
Blocadren®

Possible Sensitivity to Timolol
INFORMATIVE

CYP2D6: Intermediate Metabolizer

Potentiated systemic beta-blockade (e.g., bradycardia) has been reported during timolol treatment by patients with decreased CYP2D6 activity. Monitor patient for treatment-related adverse effects.

- Yuan H, Yu M, Yang Y, Wu K, Lin X, Li J. Association of CYP2D6 single-nucleotide polymorphism with response to ophthalmic timolol in primary open-angle Glaucoma--a pilot study. J Ocul Pharmacol Ther 2010 Oct;26(5):497-501.
- Canpolat U, Gürses KM, Aytemir K, Oto A. Severe bradycardia and syncope due to topical ophthalmic timolol. Herz 2013 Aug;38(5):556-7.

Tizanidine
Zanaflex®

Possible Non-Response to Tizanidine
INFORMATIVE

CYP1A2: Normal Metabolizer - Higher Inducibility

There is little evidence regarding the impact of CYP1A2 genetic variants on tizanidine response. Smokers may be at risk for non-response and may require higher doses. There is an association between high tizanidine plasma concentrations and the risk of hypotension and excessive sedation. Therefore, careful monitoring is recommended during dosing adjustment. Smoking cessation may increase plasma drug levels, leading to excessive hypotension and sedation. Careful monitoring accompanied by dose reduction may be needed in patients who have quit smoking.

- Backman JT, Schröder MT, Neuvonen PJ. Effects of gender and moderate smoking on the pharmacokinetics and effects of the CYP1A2 substrate tizanidine. Eur J Clin Pharmacol 2008 Jan;64(1):17-24.
- Granfors MT, Backman JT, Neuvonen M, Ahonen J, Neuvonen PJ. Fluvoxamine drastically increases concentrations and effects of tizanidine: a potentially hazardous interaction. Clin Pharmacol Ther 2004 Apr;75(4):331-41.
- Al-Ghazawi M, Alzoubi M, Faidi B. Pharmacokinetic comparison of two 4 mg tablet formulations of tizanidine. Int J Clin Pharmacol Ther 2013 Mar;51(3):255-62.
- Koonrungsesomboon N, Khatsri R, Wongchompoo P, Teekachunhatean S. The impact of genetic polymorphisms on CYP1A2 activity in humans: a systematic review and meta-analysis. Pharmacogenomics J 2018 12;18(6):760-768.

Tramadol
Ultram®

Decreased Exposure to Tramadol Active Metabolite
INFORMATIVE

CYP2D6: Intermediate Metabolizer

The patient genotype is associated with decreased conversion of tramadol to its active metabolite (O-desmethyltramadol), which may result in decreased effectiveness.

Tramadol can be prescribed at standard label-recommended age- or weight-based dosing and monitoring. If no response and opioid use is warranted, consider a non-codeine opioid. Alternative opioids may include: fentanyl, morphine, hydromorphone, oxymorphone, and tapentadol.

- Crews KR, Monte AA, Huddart R, Caudle KE, Kharasch ED, Gaedigk A, Dunnenberger HM, Leeder JS, Callaghan JT, Samer CF, Klein TE, Haidar CE, Van Driest SL, Ruano G, Sangkuhl K, Cavallari LH, Müller DJ, Prows CA, Nagy M, Somogyi AA, Skaar TC. Clinical Pharmacogenetics Implementation Consortium Guideline for CYP2D6, OPRM1, and COMT Genotypes and Select Opioid Therapy. Clin Pharmacol Ther 2021 10;110(4):888-896.

Trimipramine
Surmontil®

Increased Trimipramine Exposure
INFORMATIVE

CYP2D6: Intermediate Metabolizer

The patient is predicted to be a CYP2D6 intermediate metabolizer which is likely to result in decreased metabolism of trimipramine to less active compounds and a subsequent increase in trimipramine exposure leading to side effects.

Psychiatric Conditions: Consider a 25% reduction of the recommended dose and use therapeutic drug monitoring to guide dose adjustments.

- Hicks JK, Sangkuhl K, Swen JJ, Ellingrod VL, Müller DJ, Shimoda K, Bishop JR, Kharasch ED, Skaar TC, Gaedigk A, Dunnenberger HM, Klein TE, Caudle KE, Stingl JC. Clinical pharmacogenetics implementation consortium guideline (CPIC) for CYP2D6 and CYP2C19 genotypes and dosing of tricyclic antidepressants: 2016 update. Clin Pharmacol Ther 2017 07;102(1):37-44.

Increased Trimipramine Exposure
INFORMATIVE

CYP2D6: Intermediate Metabolizer

CYP2C19: Intermediate Metabolizer

The patient's reduced CYP2D6 activity is likely to result in decreased metabolism of trimipramine to less active compounds and a subsequent increase in trimipramine exposure leading to side effects.

Psychiatric Conditions: Consider a 25% reduction of the recommended dose and use therapeutic drug monitoring to guide dose adjustments.

- Hicks JK, Sangkuhl K, Swen JJ, Ellingrod VL, Müller DJ, Shimoda K, Bishop JR, Kharasch ED, Skaar TC, Gaedigk A, Dunnenberger HM, Klein TE, Caudle KE, Stingl JC. Clinical pharmacogenetics implementation consortium guideline (CPIC) for CYP2D6 and CYP2C19 genotypes and dosing of tricyclic antidepressants: 2016 update. Clin Pharmacol Ther 2017 07;102(1):37-44.

Vortioxetine
Trintellix®

Increased Vortioxetine Exposure
ACTIONABLE

CYP2D6: Intermediate Metabolizer

The patient's genotype is associated with an increased exposure to vortioxetine, which may increase risk of adverse effects. Vortioxetine can be prescribed at standard label-recommended dosage with close monitoring.

- Bousman CA, Stevenson JM, Ramsey LB, Sangkuhl K, Hicks JK, Strawn JR, Singh AB, Ruaño G, Mueller DJ, Tsermpini EE, Brown JT, Bell GC, Leeder JS, Gaedigk A, Scott SA, Klein TE, Caudle KE, Bishop JR. Clinical Pharmacogenetics Implementation Consortium (CPIC) Guideline for CYP2D6, CYP2C19, CYP2B6, SLC6A4, and HTR2A Genotypes and Serotonin Reuptake Inhibitor Antidepressants. Clin Pharmacol Ther. 2023 Apr 9. doi: 10.1002/cpt.2903. Epub ahead of print. PMID: 37032427.

Zonisamide
Zonegran®

Possible Sensitivity to Zonisamide
INFORMATIVE

CYP2C19: Intermediate Metabolizer

CYP2C19 is partly involved in the metabolism of zonisamide, and although preliminary studies show that CYP2C19 intermediate metabolizers have a slightly lower (15%) zonisamide clearance than normal metabolizers, no significant change in the clinical outcome has been reported with this antiepileptic drug. Therefore, zonisamide can be prescribed at standard label-recommended dosage and administration with a closer monitoring for adverse events.

- Okada Y, Seo T, Ishitsu T, Wanibuchi A, Hashimoto N, Higa Y, Nakagawa K. Population estimation regarding the effects of cytochrome P450 2C19 and 3A5 polymorphisms on zonisamide clearance. Ther Drug Monit 2008 Aug;30(4):540-3.

Sample Org
123 Street Street Greenville, SC 29615

PATIENT INFORMATION	
NAME:	test14 test14
DOB:	04/29/1962
SEX:	Female

SPECIMEN DETAILS	
SAMPLE ID:	PGT-24-001-14
SPECIMEN TYPE:	None
COLLECTION DATE:	02/21/2024
RECEIVED DATE:	02/23/2024
REPORT DATE:	05/16/2024

PROVIDER INFORMATION
PROVIDER: LOREN KIDD
FACILITY: Medical Office

Legend

Consider Alternatives: A medication has potentially reduced efficacy, increased toxicity or the patient has an increased risk for the indicated condition.

Use with Caution: Guidelines exist for adjusting dosage, increased vigilance or the patient has a moderate risk for the indicated condition.

Standard Precautions: The medication can be prescribed according to standard regimens or the patient's risk for the indicated condition is not increased.

ACTIONABLE — Recommendations based upon publications by international pharmacogenetic expert groups, consortia or regulatory bodies (CPIC, DPWG, FDA. EMA). Recommendations are suitable for implementation in a clinical setting. Guidelines may change as knowledge arises.

INFORMATIVE — There are insufficient or contradictory findings documenting the impact of a given genetic polymorphism or drug interaction. Recommendations are informative and implementation in a clinical setting is optional.

PRECISION GENETICS

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PROVIDER: LOREN KIDD
FACILITY: Medical Office

5 Test Details

Gene	Genotype	Phenotype
ABCB1	2677G>A G/G	**Variant Allele Not Present**
ABCB1	3435C>T C/T	**Heterozygous- Variant Allele Present**
ABCB1	1236T>C C/C	**Homozygous Mutant - Variant Allele Present**
ABCB1	2677G>T G/G	**Variant Allele Not Present**
ABCG2	421C>A C/C	**Normal Function**
ADRA2A	c.427A>G G/G	**Homozygous for the G allele (rs553668)**
ADRA2A	C-1291G C/C	**Homozygous for C Allele**
ADRB2	rs1042713 G/G	**Normal ADRB2 Function**
ANKK1	DRD2:Taq1A A/G	**Altered DRD2 function**
C11ORF65	rs11212617 C/A	**Heterozygous for the A allele (rs11212617)**
COMT	Val158Met A/G	**Intermediate COMT Activity**
CYP1A2	*1A/*1F	**Normal Metabolizer - Higher Inducibility**
CYP2B6	*1/*1	**Normal Metabolizer**
CYP2C19	*2/*17	**Intermediate Metabolizer**
CYP2C8	*1A/*1A	**Normal Metabolizer**
CYP2C9	*1/*1	**Normal Metabolizer**
CYP2D6	*1/*4	**Intermediate Metabolizer**
CYP3A4	*1/*1	**Normal Metabolism**
CYP3A5	*3/*3	**Poor Metabolizer**
DRD2	g.113411054A>C C/A	**Heterozygous for the A allele (rs2734841)**
DRD2	-241A>G T/T	**Homozygous for rs1799978 T allele**
EPHX1	c.337T>C T/T	**Homozygous for the T allele (rs1051740)**
F2	rs1799963 GG	**Normal Thrombosis Risk**
F5	rs6025 CC	**Normal Thrombosis Risk**
GRIK4	83-10039T>C T/C	**Reduced Response to Citalopram**

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HTR2A	rs7997012 A/G	**Heterozygous for the A allele (rs7997012)**
HTR2A	-1438G>A C/C	**Homozygous for the C allele (rs6311)**
HTR2C	-759C>T T/T	**Homozygous for the T allele**
HTR2C	114138144C>G G/G	**Homozygous for the G allele**
ITGB3	176T>C T/T	**Normal Platelet Reactivity**
MTHFR	c.1286A>C GG	**Reduced MTHFR Activity**
MTHFR	c.665C>T GG	**Normal MTHFR Activity**
NUDT15	*1/*1	**Normal Metabolizer**
OPRM1	A118G A/A	**Normal OPRM1 Function**
SLCO1B1	*1/*1	**Normal Function**
TPMT	*1/*3A or *3B/*3C	**Poor or Intermediate Metabolizer**
UGT2B15	*2/*2	**Poor Function**
VKORC1	-1639G>A G/A	**Intermediate Warfarin Sensitivity**

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 : This test interrogates 120 SNPs within drug metabolism enzymes and associated transporter genes. The assay provides coverage of essential, commonly studied markers within CYP2D6, CYP2C9, CYP2C19, and other important drug metabolism enzymes and clinical research genes. Each SNP genotyping assay in the panel contains two allele-specific probes and a primer pair to detect the specific SNP target. Both the probes and primers uniquely align within the genome. Array based assays detect listed alleles, including all common and most rare variants with known clinical significance at analytical sensitivity and specificity >99%.

Lab Disclaimer: Lab developed the Comprehensive PGx Panel. The performance characteristics of this test were determined by Lab. It has not been cleared or approved by the U.S. Food and Drug Administration.

Reported By:

Brooks Morrison *2024-05-16 03:30 PM UTC*