CLIA # 18D1100471
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PATIENT INFORMATION		PHYSICIAN		SPECIMEN DETAILS	
Name:	**Jenny Doe**	Provider:	**Seuss, Theodore**	Specimen ID:	**210930157674**
Patient ID:	**P12345678**	Location:	**ABC Clinic**	Specimen Type:	**Buccal**
DOB:	**01/01/1970**	Client #:	**12345**	Collection Date:	**04/28/2021**
SEX:	**Female**	Phone:	**859-867-5309**	Received Date:	**04/27/2021**
				Report Date:	**10/04/2021**

Order Choice: *GetMyDNA PWN*

Substantial Drug-Gene Interaction
Genetic information should be strongly considered to change the prescribing of the indicated medication due to an increased risk of adverse reactions or a reduction in efficacy.

Moderate Drug-Gene Interaction
Genetic information should be considered as the identified medication may have an increased risk of adverse reactions or a reduction in efficacy.

Limited Drug-Gene Interaction
The standard precautions for prescribing the indication medication should be followed.

LEVEL OF EVIDENCE

FDA: The FDA labeling for the identified drug may contain specific actions to be taken based on genetic information. There may be alleles not accounted for based on the inferred phenotypes.

CPIC Level A: Preponderance of evidence is high or moderate in favor of changing prescribing of identified drug based on genetic information.

CPIC Level B: Preponderance of evidence is weak with little conflicting data in favor of changing prescribing of identified drug based on genetic information and alternative therapies/dosing are extremely likely to be as effective and as safe as non-genetically based dosing.

CPIC Level C: There are published studies at varying levels of evidence, some with mechanistic rationale, but no prescribing actions are recommended.

The reported drug-gene interactions are based on consensus scientific evidence referenced from the dosing guidelines on the FDA label or the Clinical Pharmacogenetics Implementation Consortium (CPIC) recommendations. This report is intended to aid healthcare providers in determining the proper treatment options for a patient and should be used in the context of other clinical factors to change or select medications and dosage.

! Please note: Do not make any changes to your medication without consulting a physician.

Current Patient Medications

Ondansetron, Clomipramine, Desipramine, Sertraline

Clomipramine | Psychiatry
CYP2D6 Poor Metabolizer — CPIC Level B, FDA

Desipramine | Psychiatry
CYP2D6 Poor Metabolizer — CPIC Level B, FDA

Ondansetron | Gastroenterology
CYP2D6 Poor Metabolizer — CPIC Level A, FDA

Sertraline | Psychiatry
CYP2C19 Normal (Extensive) Metabolizer — CPIC Level B

Potentially Impacted Medications

Cardiovascular

	Substantial Drug-Gene Interaction	Moderate Drug-Gene Interaction	Limited Drug-Gene Interaction
Antiarrhythmics		Propafenone	
Anticoagulants		Warfarin	Acenocoumarol
Antiplatelets			Clopidogrel
Beta Blockers		Carvedilol Metoprolol Nebivolol Propranolol	
Statins			Simvastatin
Thrombopoietin Receptor Agonists			Avatrombopag

Gastroenterology

	Substantial Drug-Gene Interaction	Moderate Drug-Gene Interaction	Limited Drug-Gene Interaction
Antiemetics		Ondansetron Metoclopramide	Dronabinol
Proton Pump Inhibitors			Omeprazole Lansoprazole Pantoprazole Dexlansoprazole Esomeprazole Rabeprazole

Gynecology

	Substantial Drug-Gene Interaction	Moderate Drug-Gene Interaction	Limited Drug-Gene Interaction
Gynecology Pain Medication			Elagolix
HSDD Agents-Mixed Serotonin Agonist/Antagonists			Flibanserin

Infectious Diseases

	Substantial Drug-Gene Interaction	Moderate Drug-Gene Interaction	Limited Drug-Gene Interaction
Anti-Fungal Drugs			Voriconazole
Anti-HIV Drugs		Efavirenz	

Neurology

	Substantial Drug-Gene Interaction	Moderate Drug-Gene Interaction	Limited Drug-Gene Interaction
Anticonvulsants			Brivaracetam Phenytoin Fosphenytoin
Benzodiazepines			Clobazam Diazepam
Cholinesterase Inhibitors		Donepezil Galantamine	
Movement Disorder Therapy		Deutetrabenazine Tetrabenazine Valbenazine	
Multiple Sclerosis Treatment			Siponimod
Vertigo Treatment		Meclizine	

Oncology

	Substantial Drug-Gene Interaction	Moderate Drug-Gene Interaction	Limited Drug-Gene Interaction
Antineoplastic	Tamoxifen	Gefitinib	Erdafitinib

Other

	Substantial Drug-Gene Interaction	Moderate Drug-Gene Interaction	Limited Drug-Gene Interaction
Dental		Cevimeline	
Metabolic Modifier		Eliglustat	
Immunosuppressive			Tacrolimus

Pain Management

	Substantial Drug-Gene Interaction	Moderate Drug-Gene Interaction	Limited Drug-Gene Interaction
Analgesic Opioid	Codeine Hydrocodone Tramadol	Methadone Oliceridine	
NSAID			Lornoxicam Meloxicam Tenoxicam

Psychiatry

	Substantial Drug-Gene Interaction	Moderate Drug-Gene Interaction	Limited Drug-Gene Interaction
ADHD Therapy		Atomoxetine Amphetamine	
Antiaddictives		Lofexidine	
Antidepressant	Doxepin Amitriptyline Clomipramine Imipramine Trimipramine Fluvoxamine Amoxapine Desipramine Nortriptyline Paroxetine	Protriptyline Venlafaxine Vortioxetine	Escitalopram Citalopram Sertraline
Antipsychotics		Aripiprazole Aripiprazole Lauroxil Brexpiprazole Clozapine Iloperidone Perphenazine Pimozide Thioridazine Risperidone	
Narcolepsy Therapy Agents		Pitolisant	

Rheumatology

	Substantial Drug-Gene Interaction	Moderate Drug-Gene Interaction	Limited Drug-Gene Interaction
Muscle Relaxant			Carisoprodol
NSAID Analgesic			Celecoxib Flurbiprofen Piroxicam

Urology

	Substantial Drug-Gene Interaction	Moderate Drug-Gene Interaction	Limited Drug-Gene Interaction
Alpha Blocker		Tamsulosin	
Urinary Antispasmodic		Darifenacin Fesoterodine Mirabegron Tolterodine	

Dosing Guidance

✕ Tamoxifen | Antineoplastic — CPIC Level A, FDA

CYP2D6 Poor Metabolizer

Implications: Lower endoxifen concentrations compared to Normal (Extensive) Metabolizers; higher risk of breast cancer recurrence, event-free and recurrence-free survival compared to Normal (Extensive) Metabolizers.

Therapeutic Recommendations: Recommend alternative hormonal therapy such as an aromatase inhibitor for postmenopausal women or aromatase inhibitor along with ovarian function suppression in premenopausal women given that these approaches are superior to tamoxifen regardless of CYP2D6 genotype and based on knowledge that CYP2D6 poor metabolizers switched from tamoxifen to anastrozole do not have an increased risk of recurrence. Note, higher dose tamoxifen increases but does not normalize endoxifen concentrations and can be considered if there are contraindications to aromatase inhibitor therapy.

✕ Paroxetine | Antidepressant — CPIC Level A, FDA

CYP2D6 Poor Metabolizer

Implications: Greatly reduced metabolism when compared to Normal (Extensive) Metabolizers. Higher plasma concentrations may increase the probability of side effects.

Therapeutic Recommendations: Select alternative drug not predominantly metabolized by CYP2D6 or if paroxetine use warranted, consider a 50% reduction of recommended starting dose and titrate to response.

✕ Fluvoxamine | Antidepressant — CPIC Level B, FDA

CYP2D6 Poor Metabolizer

Implications: Greatly reduced metabolism when compared to Normal (Extensive) Metabolizers. Higher plasma concentrations may increase the probability of side effects.

Therapeutic Recommendations: Consider a 25–50% reduction of recommended starting dose and titrate to response or use an alternative drug not metabolized by CYP2D6.

✕ Codeine | Analgesic Opioid — CPIC Level A, FDA

CYP2D6 Poor Metabolizer

Implications: Greatly reduced morphine formation leading to diminished analgesia.

Therapeutic Recommendations: Avoid codeine use because of possibility of diminished analgesia. If opioid use is warranted, consider a non-tramadol opioid.

✕ Tramadol | Analgesic Opioid — CPIC Level A, FDA

CYP2D6 Poor Metabolizer

Implications: Greatly reduced O-desmethyltramadol (active metabolite) formation leading to diminished analgesia.

Therapeutic Recommendations: Avoid tramadol use because of possibility of diminished analgesia. If opioid use is warranted, consider a non codeine opioid.

✕ Hydrocodone | Analgesic Opioid — CPIC Level B

CYP2D6 Poor Metabolizer

Implications: Decreased metabolism of hydrocodone to active metabolite, hydromorphone, but there is insufficient evidence to determine if these effects on pharmacokinetics translate into decreased analgesia or side effects.

Therapeutic Recommendations: Use hydrocodone label recommended age-specific or weight-specific dosing. If no response and opioid use is warranted, consider non-codeine and non-tramadol opioid.

✕ Amitriptyline | Antidepressant — CPIC Level A, FDA

CYP2D6 Poor Metabolizer

Implications: Greatly reduced metabolism of TCAs to less active compounds compared to Normal (Extensive) Metabolizers. Higher plasma concentrations of active drug will increase the probability of side effects.

Therapeutic Recommendations: Avoid tricyclic use due to potential for side effects. Consider alternative drug not metabolized by CYP2D6. If a TCA is warranted, consider a 50% reduction of recommended starting dose. Utilize therapeutic drug monitoring to guide dose adjustments.

✕ Amoxapine | Antidepressant — CPIC Level B/C, FDA

CYP2D6 Poor Metabolizer

Implications: The biochemical activity of the drug metabolizing isozyme CYP2D6 is reduced in poor metabolizers. Poor metabolizers have higher than expected plasma concentrations of tricyclic antidepressants (TCAs) when given usual doses.

Therapeutic Recommendations: Potential for abnormal therapeutic response at standard dose. Amoxapine should be used with caution in patients with reduced CYP2D6 activity.

✕ Clomipramine | Antidepressant — CPIC Level B, FDA

CYP2D6 Poor Metabolizer

Implications: Greatly reduced metabolism of TCAs to less active compounds compared to Normal (Extensive) Metabolizers. Higher plasma concentrations of active drug will increase the probability of side effects.

Therapeutic Recommendations: Avoid tricyclic use due to potential for side effects. Consider alternative drug not metabolized by CYP2D6. If a TCA is warranted, consider a 50% reduction of recommended starting dose. Utilize therapeutic drug monitoring to guide dose adjustments.

✕ Desipramine | Antidepressant — CPIC Level B, FDA

CYP2D6 Poor Metabolizer

Implications: Greatly reduced metabolism of TCAs to less active compounds compared to Normal (Extensive) Metabolizers. Higher plasma concentrations of active drug will increase the probability of side effects.

Therapeutic Recommendations: Avoid tricyclic use due to potential for side effects. Consider alternative drug not metabolized by CYP2D6. If a TCA is warranted, consider a 50% reduction of recommended starting dose. Utilize therapeutic drug monitoring to guide dose adjustments.

✕ Doxepin | Antidepressant — CPIC Level B, FDA

CYP2D6 Poor Metabolizer

Implications: Greatly reduced metabolism of TCAs to less active compounds compared to Normal (Extensive) Metabolizers. Higher plasma concentrations of active drug will increase the probability of side effects.

Therapeutic Recommendations: Avoid tricyclic use due to potential for side effects. Consider alternative drug not metabolized by CYP2D6. If a TCA is warranted, consider a 50% reduction of recommended starting dose. Utilize therapeutic drug monitoring to guide dose adjustments.

✕ Imipramine | Antidepressant — CPIC Level B, FDA

CYP2D6 Poor Metabolizer

Implications: Greatly reduced metabolism of TCAs to less active compounds compared to Normal (Extensive) Metabolizers. Higher plasma concentrations of active drug will increase the probability of side effects.

Therapeutic Recommendations: Avoid tricyclic use due to potential for side effects. Consider alternative drug not metabolized by CYP2D6. If a TCA is warranted, consider a 50% reduction of recommended starting dose. Utilize therapeutic drug monitoring to guide dose adjustments.

✕ Nortriptyline | Antidepressant — CPIC Level A, FDA

CYP2D6 Poor Metabolizer

Implications: Greatly reduced metabolism of TCAs to less active compounds compared to Normal (Extensive) Metabolizers. Higher plasma concentrations of active drug will increase the probability of side effects.

Therapeutic Recommendations: Avoid tricyclic use due to potential for side effects. Consider alternative drug not metabolized by CYP2D6. If a TCA is warranted, consider a 50% reduction of recommended starting dose. Utilize therapeutic drug monitoring to guide dose adjustments.

✕ Trimipramine | Antidepressant — CPIC Level B, FDA

CYP2D6 Poor Metabolizer

Implications: Greatly reduced metabolism of TCAs to less active compounds compared to Normal (Extensive) Metabolizers. Higher plasma concentrations of active drug will increase the probability of side effects.

Therapeutic Recommendations: Avoid tricyclic use due to potential for side effects. Consider alternative drug not metabolized by CYP2D6. If a TCA is warranted, consider a 50% reduction of recommended starting dose. Utilize therapeutic drug monitoring to guide dose adjustments.

••• Efavirenz | Anti-HIV Drugs — CPIC Level A, FDA

CYP2B6 Intermediate Metabolizer

Implications: Higher dose-adjusted trough concentrations of efavirenz compared with Normal (Extensive) Metabolizers; increased risk of CNS adverse events.

Therapeutic Recommendations: Consider initiating efavirenz with a decreased dose.

Methadone | Analgesic Opioid — CPIC Level B

CYP2B6 Intermediate Metabolizer

Implications: Patients with one copy of the *6 allele (e.g. *1/*6) may have decreased methadone clearance compared to patients without the *6 allele.

Therapeutic Recommendations: No recommendation based on CYP2B6 genotype.

Warfarin | Anticoagulants — CPIC Level A, FDA

VKORC1 Increased Warfarin Sensitivity

Implications: A common variant upstream of VKORC1 rs9923231 is significantly associated with warfarin sensitivity and patients with one or two T alleles require progressively lower warfarin doses than those homozygous for the C allele.

Therapeutic Recommendations: Patients with one or two T alleles require progressively lower warfarin doses.

Atomoxetine | ADHD Therapy — CPIC Level A, FDA

CYP2D6 Poor Metabolizer

Implications: Significantly decreased metabolism of atomoxetine may result in higher concentrations as compared to non-poor metabolizers. This may increase the occurrence of side effects, but also a greater improvement of ADHD symptoms as compared with non-poor metabolizers in those who tolerate treatment. Poor metabolizer status is associated with lower final dose requirements as compared to non-poor metabolizers.

Therapeutic Recommendations: If no clinical response and in the absence of adverse events after 2 weeks, consider obtaining a plasma concentration 2–4 hours after dosing. If unacceptable side effects are present at any time, consider a reduction in dose.

Ondansetron | Antiemetics — CPIC Level A, FDA

CYP2D6 Poor Metabolizer

Implications: Very limited data is available for CYP2D6 PMs.

Therapeutic Recommendations: Insufficient evidence demonstrating clinical impact based on CYP2D6 genotype. Initiate therapy with recommended starting dose.

Amphetamine | ADHD Therapy — CPIC Level B/C, FDA

CYP2D6 Poor Metabolizer

Implications: Since CYP2D6 is genetically polymorphic, population variations in amphetamine metabolism are a possibility.

Therapeutic Recommendations: No recommendation based on CYP2D6 genotype.

Aripiprazole | Antipsychotics — CPIC Level B, FDA

CYP2D6 Poor Metabolizer

Implications: For CYP2D6 poor metabolizers, the mean elimination half-life for aripiprazole is about 146 hours.

Therapeutic Recommendations: Results in higher systemic concentrations and higher adverse reaction risk. Dosage adjustment is recommended. Refer to FDA labeling for specific dosing recommendations.

··· Aripiprazole Lauroxil | Antipsychotics — CPIC Level B/C, FDA

CYP2D6 Poor Metabolizer

Implications: Dosage adjustment is recommended in known CYP2D6 poor metabolizers due to high aripiprazole concentrations.

Therapeutic Recommendations: Results in higher systemic concentrations. Dosage adjustment is recommended. Refer to FDA labeling for specific dosing recommendations.

··· Brexpiprazole | Antipsychotics — CPIC Level B/C, FDA

CYP2D6 Poor Metabolizer

Implications: Dosage adjustment is recommended in known CYP2D6 poor metabolizers, because these patients have higher brexpiprazole concentrations than Normal (Extensive) Metabolizers of CYP2D6.

Therapeutic Recommendations: Administer half of the usual dose.

··· Carvedilol | Beta Blockers — CPIC Level B/C, FDA

CYP2D6 Poor Metabolizer

Implications: Results in higher systemic concentrations and higher adverse reaction risk (dizziness).

Therapeutic Recommendations: Potential for abnormal therapeutic response at standard dose.

··· Cevimeline | Dental — CPIC Level B/C, FDA

CYP2D6 Poor Metabolizer

Implications: Potential for a greater exposure to standard doses of cevimeline due to decreased metabolism.

Therapeutic Recommendations: Cevimeline should be used with caution in individuals known or suspected to be deficient in CYP2D6 activity, based on previous experience, as they may be at a higher risk of adverse events.

··· Clozapine | Antipsychotics — CPIC Level B/C, FDA

CYP2D6 Poor Metabolizer

Implications: Potential for a greater exposure to standard doses of clozapine due to decreased metabolism.

Therapeutic Recommendations: Dose reduction may be necessary in patients who are CYP2D6 poor metabolizers. Clozapine concentrations may be increased in these patients, because clozapine is almost completely metabolized and then excreted.

··· Darifenacin | Urinary Antispasmodic — CPIC Level C, FDA

CYP2D6 Poor Metabolizer

Implications: Potential for a greater exposure to standard doses of darifenacin due to decreased metabolism.

Therapeutic Recommendations: Potential for abnormal therapeutic response at standard dose.

Deutetrabenazine | Movement Disorder Therapy — CPIC Level B/C, FDA

CYP2D6 Poor Metabolizer

Implications: Although the pharmacokinetics of deutetrabenazine and its metabolites have not been systematically evaluated in patients who do not express the drug metabolizing enzyme, it is likely that the exposure to α-HTBZ and β-HTBZ would be increased similarly to taking a strong CYP2D6 inhibitor (approximately 3- fold).

Therapeutic Recommendations: Results in higher systemic concentrations and adverse reaction risk (QT prolongation). The maximum recommended dosage should not exceed 36 mg (maximum single dose of 18 mg).

Donepezil | Cholinesterase Inhibitors — CPIC Level B/C, FDA

CYP2D6 Poor Metabolizer

Implications: Examination of the effect of CYP2D6 genotype in Alzheimer's patients showed differences in clearance values among CYP2D6 genotype subgroups. When compared to the Normal (Extensive) Metabolizers, poor metabolizers had a 31.5% slower clearance.

Therapeutic Recommendations: Potential for abnormal therapeutic response at standard dose.

Eliglustat | Metabolic Modifier — CPIC Level A/B, FDA

CYP2D6 Poor Metabolizer

Implications: Potential for a greater eliglustat exposure to standard doses due to decreased metabolism and clearance.

Therapeutic Recommendations: Indicated for normal, intermediate, and poor metabolizer patients. Coadministration with strong CYP3A inhibitors is contraindicated in intermediate and poor CYP2D6 metabolizers.

Fesoterodine | Urinary Antispasmodic — CPIC Level C, FDA

CYP2D6 Poor Metabolizer

Implications: Potential for a greater fesoterodine exposure to standard doses due to decreased metabolism and clearance.

Therapeutic Recommendations: No recommendation based on CYP2D6 genotype.

Galantamine | Cholinesterase Inhibitors — CPIC Level C, FDA

CYP2D6 Poor Metabolizer

Implications: Results in higher systemic concentrations.

Therapeutic Recommendations: Dosage adjustment is not necessary in patients identified as poor metabolizers as the dose of drug is individually titrated to tolerability.

··· Gefitinib | Antineoplastic — CPIC Level B/C, FDA

CYP2D6 Poor Metabolizer

Implications: In healthy CYP2D6 poor metabolizers, O-desmethyl gefitinib concentration was not measurable and the mean exposure to gefitinib was 2-fold higher as compared to the Normal (Extensive) Metabolizers. This increase in exposure in CYP2D6 poor metabolizers may be clinically important because some adverse drug reactions are related to higher exposure of gefitinib.

Therapeutic Recommendations: No dose adjustment is recommended in patients with a known CYP2D6 poor metabolizer genotype, but these patients should be closely monitored for adverse reactions.

··· Iloperidone | Antipsychotics — CPIC Level B/C, FDA

CYP2D6 Poor Metabolizer

Implications: Potential for a greater iloperidone exposure to standard doses due to decreased metabolism and clearance.

Therapeutic Recommendations: Iloperidone dose should be reduced by one-half for poor metabolizers of CYP2D6.

··· Lofexidine | Antiaddictives — CPIC Level B/C, FDA

CYP2D6 Poor Metabolizer

Implications: Although the pharmacokinetics of lofexidine have not been systematically evaluated in patients who do not express the drug metabolizing enzyme CYP2D6, it is likely that the exposure to lofexidine would be increased similarly to taking strong CYP2D6 inhibitors (approximately 28%).

Therapeutic Recommendations: Monitor adverse events such as orthostatic hypotension and bradycardia in known CYP2D6 poor metabolizers.

··· Meclizine | Vertigo Treatment — CPIC Level B/C, FDA

CYP2D6 Poor Metabolizer

Implications: The genetic polymorphism of CYP2D6 that results in poor-, intermediate-, extensive-, and ultrarapid metabolizer phenotypes could contribute to large inter-individual variability in meclizine exposure.

Therapeutic Recommendations: When meclizine is administered to patients with CYP2D6 polymorphism, monitor for adverse reactions and clinical effect accordingly.

··· Metoclopramide | Antiemetics — CPIC Level B/C, FDA

CYP2D6 Poor Metabolizer

Implications: The elimination of metoclopramide may be slowed in patients who are CYP2D6 poor metabolizers (compared to patients who are CYP2D6 intermediate, extensive, or ultra-rapid metabolizers); possibly increasing the risk of dystonic and other adverse reactions to metoclopramide.

Therapeutic Recommendations: Reduce the metoclopramide dosage in patients who are poor CYP2D6 metabolizers.

Metoprolol | Beta Blockers — CPIC Level B/C, FDA

CYP2D6 Poor Metabolizer

Implications: Poor metabolizers, intermediate metabolizers and Normal (Extensive) Metabolizers who concomitantly use CYP2D6 inhibiting drugs will have increased (several-fold) metoprolol blood levels, decreasing metoprolol's cardioselectivity.

Therapeutic Recommendations: Potential for abnormal therapeutic response at standard dose.

Mirabegron | Urinary Antispasmodic — CPIC Level B/C, FDA

CYP2D6 Poor Metabolizer

Implications: Results in higher systemic concentrations.

Therapeutic Recommendations: Potential for abnormal therapeutic response at standard dose.

Nebivolol | Beta Blockers — CPIC Level B/C, FDA

CYP2D6 Poor Metabolizer

Implications: May result in higher systemic concentrations.

Therapeutic Recommendations: No dose adjustments are necessary for patients who are CYP2D6 poor metabolizers. The clinical effect and safety profile observed in poor metabolizers were similar to those of Normal (Extensive) Metabolizers.

Perphenazine | Antipsychotics — CPIC Level B/C, FDA

CYP2D6 Poor Metabolizer

Implications: Poor metabolizers of CYP 2D6 will metabolize perphenazine more slowly and will experience higher concentrations compared with normal or metabolizers.

Therapeutic Recommendations: No recommendation.

Pimozide | Antipsychotics — CPIC Level A/B, FDA

CYP2D6 Poor Metabolizer

Implications: Individuals with genetic variations resulting in poor CYP2D6 metabolism exhibit higher pimozide concentrations than Normal (Extensive) Metabolizers. The concentrations observed in CYP2D6 poor metabolizers are similar to those seen with strong CYP2D6 inhibitors such as paroxetine. The time to achieve steady state pimozide concentrations is expected to be longer (approximately 2 weeks) in CYP2D6 poor metabolizers because of the prolonged half-life.

Therapeutic Recommendations: Alternative dosing strategies are recommended in patients who are genetically CYP2D6 poor metabolizers.

Pitolisant | Narcolepsy Therapy Agents — CPIC Level A, FDA

CYP2D6 Poor Metabolizer

Implications: Results in higher systemic concentrations.

Therapeutic Recommendations: Dosage reduction is recommended in patients known to be poor CYP2D6 metabolizers because these patients have higher pitolisant concentrations than normal CYP2D6 metabolizers.

Propafenone | Antiarrhythmics — CPIC Level B/C, FDA

CYP2D6 Poor Metabolizer

Implications: Results in higher systemic concentrations and higher adverse reaction risk (arrhythmia). Avoid use in poor metabolizers taking a CYP3A4 inhibitor.

Therapeutic Recommendations: Because the difference decreases at high doses and is mitigated by the lack of the active 5-hydroxy metabolite in the slow metabolizers, and because steady-state conditions are achieved after for to five days of dosing in all patients, the recommended dosing regimen of propafenone is the same for all patients. The large intersubject variability in blood levels require that the dose of the drug be titrated carefully in patients with close attention paid to clinical and ECG evidence of toxicity.

Propranolol | Beta Blockers — CPIC Level B/C, FDA

CYP2D6 Poor Metabolizer

Implications: May affect systemic concentrations.

Therapeutic Recommendations: No recommendation based on CYP2D6 genotype.

Protriptyline | Antidepressant — CPIC Level B/C, FDA

CYP2D6 Poor Metabolizer

Implications: Poor metabolizers have higher than expected plasma concentrations of tricyclic antidepressants (TCAs) when given usual doses.

Therapeutic Recommendations: No recommendation based on CYP2D6 genotype.

Risperidone | Antipsychotics — CPIC Level B, FDA

CYP2D6 Poor Metabolizer

Implications: Peak concentrations of 9-hydroxyrisperidone occurred at about 3 hours in Normal (Extensive) Metabolizers, and 17 hours in poor metabolizers. Steady-state concentrations of risperidone are reached in 1 day in Normal (Extensive) Metabolizers and would be expected to reach steady-state in about 5 days in poor metabolizers.

Therapeutic Recommendations: No recommendation based on CYP2D6 genotype.

Tamsulosin | Alpha Blocker — CPIC Level B/C, FDA

CYP2D6 Poor Metabolizer

Implications: Results in higher systemic concentrations. Predicted effect based on experience with CYP2D6 inhibitors. Use with caution.

Therapeutic Recommendations: No recommendation based on CYP2D6 genotype.

Tetrabenazine | Movement Disorder Therapy — CPIC Level A/B, FDA

CYP2D6 Poor Metabolizer

Implications: Although the pharmacokinetics of tetrabenazine and its metabolites in patients who do not express the drug metabolizing enzyme, CYP2D6, poor metabolizers, (PMs), have not been systematically evaluated, it is likely that the exposure to α-HTBZ and β-HTBZ would be increased similar to that observed in patients taking strong CYP2D6 inhibitors (3- and 9-fold, respectively).

Therapeutic Recommendations: Results in higher systemic concentrations. The dosage should, therefore, be adjusted according to a patient's CYP2D6 metabolizer status.

Thioridazine | Antipsychotics — CPIC Level B/C, FDA

CYP2D6 Poor Metabolizer

Implications: Results in higher systemic concentrations and higher adverse reaction risk (QT prolongation). Predicted effect based on experience with CYP2D6 inhibitors. Contraindicated in poor metabolizers.

Therapeutic Recommendations: Contraindicated in poor metabolizers.

Tolterodine | Urinary Antispasmodic — CPIC Level C, FDA

CYP2D6 Poor Metabolizer

Implications: Results in higher systemic concentrations and higher adverse reaction risk (QT prolongation).

Therapeutic Recommendations: No recommendation based on CYP2D6 genotype.

Valbenazine | Movement Disorder Therapy — CPIC Level B/C, FDA

CYP2D6 Poor Metabolizer

Implications: Increased exposure (Cmax and AUC) to valbenazine's active metabolite is anticipated in CYP2D6 poor metabolizers. Increased exposure of active metabolite may increase the risk of exposure-related adverse reactions.

Therapeutic Recommendations: Consider reducing valbenazine dose based on tolerability for known CYP2D6 poor metabolizers. Increased exposure (Cmax and AUC) to valbenazine's active metabolite is anticipated in CYP2D6 poor metabolizers. Increased exposure of active metabolite may increase the risk of exposure-related adverse reactions.

Venlafaxine | Antidepressant — CPIC Level A/B, FDA

CYP2D6 Poor Metabolizer

Implications: CYP2D6 poor metabolizers had increased levels of venlafaxine and reduced levels of the metabolite ODV compared to people with normal CYP2D6 levels (Normal (Extensive) Metabolizers).

Therapeutic Recommendations: Consider dosage reductions.

••• Vortioxetine | Antidepressant — CPIC Level A/B, FDA

CYP2D6 Poor Metabolizer

Implications: CYP2D6 is the primary enzyme catalyzing the metabolism of vortioxetine to its major, pharmacologically inactive, carboxylic acid metabolite, and poor metabolizers of CYP2D6 have approximately twice the vortioxetine plasma concentration of Normal (Extensive) Metabolizers.

Therapeutic Recommendations: The maximum recommended dose of vortioxetine is 10 mg/day in known CYP2D6 poor metabolizers.

••• Oliceridine | Analgesic Opioid — CPIC Level A/B

CYP2D6 Poor Metabolizer

Implications: In healthy subjects who are CYP2D6 poor metabolizers, the AUC of oliceridine was approximately 2-fold higher than in subjects who are nonpoor CYP2D6 metabolizers.

Therapeutic Recommendations: In patients who are known or suspected to be poor CYP2D6 metabolizers, based on genotype or previous history/experience with other CYP2D6 substrates, less frequent dosing of Oliceridine may be required. These patients should be closely monitored, and subsequent doses should be based on the patient's severity of pain and response to treatment.

Test Details

Gene	Genotype	Phenotype
CYP1A2	*1A/*1F	Rapid Metabolizer
CYP2B6	*1/*7	Intermediate Metabolizer
CYP2C19	*1/*1	Normal (Extensive) Metabolizer
CYP2C9	*1/*1	Normal (Extensive) Metabolizer
CYP2D6	*4/*4 3N+	Poor Metabolizer
CYP3A4	*1/*1	Normal (Extensive) Metabolizer
CYP3A5	*3/*3	Poor Metabolizer
SLC6A4	S/Lg	Low Serotonin Transporter Expression

Gene	Result	Phenotype
ADRA2A		
rs1800544	G/C	Heterozygous for the G/C alleles
COMT		
rs4680	A/A	Homozygous for the A allele
F2		
rs1799963	G/G	Homozygous for the G allele (Normal)
F5		
rs6025	C/C	Homozygous for the C allele (Normal)
HTR2A		
rs6311	C/T	Heterozygous for the C/T alleles
rs7997012	A/G	Heterozygous for the A/G alleles
OPRM1		
rs1799971	A/G	Heterozygous for the A/G alleles
SLCO1B1		
rs4149056	T/T	Normal
VKORC1		
rs9923231	C/T	Increased Warfarin Sensitivity

Limitation: The information presented in this report is for medical professionals and does not constitute medical advice for the diagnosis or treatment of a patient. The medical professional is solely responsible for the treatment of the patient. This test does not detect all alleles known to result in altered or inactive function. This test does not account for all variations that may be present in the individual tested. Absence of a detectable variant does not rule out the possibility that a patient carries undetected polymorphisms that may confer a phenotype other than that reported. Phenotypes are also affected by factors such as drug-drug interactions, comorbidities, and lifestyle habits.

Methodology: Genomic DNA was extracted from buccal swabs or EDTA blood as indicated by the sample type listed on the first page of the report. Testing was performed using MassARRAY® technology (Agena Biosciences) for all tests except SLC6A4, which was performed by PCR-RFLP analysis using MspI restriction endonuclease. The alleles tested are: **ADRA2A** rs1800544; **COMT** rs4680; **CYP1A2** *1A *1C *1F *1K *1L *1E *7 *11; **CYP2B6** *1 *4*5 *6 *7 *18; **CYP2C19** *1 *2 *3 *4A *4B *5 *6 *7 *8 *9 *10 *17; **CYP2C9** *1 *2 *3 *4 *5 *6 *8 *11 *12 *13 *15 *25 *27; **CYP2D6** *1 *2 *3 *4 *5 (Deletion) *6*7 *8 *9 *10 *11 *12 *14A *14B *15 *17 *18 *19 *20 *29 *41 *69 xN(Duplication); **CYP3A4** *1 *1B *2 *17 *22; **CYP3A5** *1A *2 *3 *6 *7; **F2** rs1799963; **F5** rs6025; **HTR2A** rs7997012 rs6311; **OPRM1** rs1799971; **SLC6A4** S La Lg; **SLCO1B1** rs4149056; **VKORC1** rs9923231; In the rare instances that multiple alleles could be inferred based on the observed data, the allele with the highest population frequency will be reported.

Lab Disclaimer: Gravity Diagnostics developed and determined the performance characteristics of this laboratory-developed genotype test. It has not been reviewed or approved by the U.S. Food and Drug Administration. The information is this report is provided for clinical use, and not as an investigational or research use only. However, the educational information provided needs the appropriate clinical context of the patient and is not a substitute for clinical monitoring by a medical professional.