Sonic Genetics
Douglass Hanly Moir Pathology

Pgx OneTesting

LAB ID **250242404** DOB **02/02/1967** **(51Y Male)**
Referring Doctor Macquarie Park Biochem Qc Officer
Your ref.
Address EPPING NSW 2121
Phone
Requested 25 Oct 2018
Collected 25 Oct 2018 06:00 am
Received 25 Oct 2018 12:54 pm
Reported 30 Oct 2018 13:00 pm

Macquarie Park Biochem Qc Officer V833
Douglass Hanly Moir Path DHM/---/---/---/---
Biochemistry Dept
14 Giffnock Avenue
MACQUARIE PARK NSW 2113

Sonic PGx

Pharmacogenetic Drug-Drug Interaction Report

Interpreting this report

This report is divided into four sections for easy navigation.

1. Current patient medications
2. Potentially impacted medications
3. Dosing guidance
4. Test details - patient drug metabolism genotype results

Please note: Section 1 is of the most immediate importance. Sections 2 and 3 provide a comprehensive outline of other drugs and their potential impacts, and are intended as a reference tool for future prescribing.

Clinical notes

Added Morphine

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Comprehensive Pharmacogenetic Report

1 Current Patient Medications

Amoxapine

Possible Sensitivity to Amoxapine (CYP2D6: Poor Metabolizer) **INFORMATIVE**

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.

Morphine

Good Response to Morphine (OPRM1: Normal OPRM1 Function) **INFORMATIVE**

The patient does not carry the OPRM1 118A>G variant. Acute postoperative and cancer pain: the patient is expected to experience good analgesia at standard morphine doses. The dosing regimen needs to be individualized for each patient, taking into account the patient's prior analgesic treatment experience.

Unrecognized Medications: None

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Highly elevated risk for indicated condition or adverse drug reaction. Medication can be prescribed with monitoring; alternative therapy may be needed.

Moderately elevated risk for indicated condition or adverse drug reaction. Medication can be prescribed with monitoring; therapy adjustment may be needed.

Typical risk for indicated condition or adverse drug reaction. Medication can be prescribed according to standard dosing guidelines.

PHARMACOGENETIC RESULTS

DRUG-DRUG INTERACTIONS

ACTIONABLE	Recommendations are suitable for implementation in a clinical setting. Recommendations extracted from evidence based guidelines issued by international pharmacogenetic consortia, professional societies or regulatory bodies (CPIC, DPWG, FDA, EMA, CPNDA, ACMG).
INFORMATIVE	Recommendations are informative and implementation in a clinical setting is optional. The evidence documenting these drug-gene associations may be limited or insufficient and may require further investigation. There are no established evidence based guidelines issued by international pharmacogenetic consortia, professional societies or regulatory bodies.
MODERATE	Drug interactions of moderate severity. The clinician should assess the patient's characteristics and take action as needed.
SERIOUS	Severe drug interaction or contraindicated drug combination which may produces serious consequences in most patients. This drug combination generally should not be dispensed or administered to the same patient. Action is required to reduce risk of severe adverse interaction.

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2 Potentially Impacted Medications

CLASS	DRUG*	PHARMACOGENETIC RESULTS	INTERACTING DRUGS
5-Alpha Reductase Inhibitors for Benign Prostatic Hyperplasia	*Dutasteride*	✓	
	Finasteride	✓	
Alpha-Blockers for Benign Prostatic Hyperplasia	*Alfuzosin*	✓	
	Doxazosin	✓	
	Silodosin	✓	
	Tamsulosin	!	
	Terazosin	✓	
Angiotensin II Receptor Antagonists	Azilsartan	✓	
	Candesartan	✓	
	Eprosartan	✓	
	Irbesartan	✓	
	Losartan	✓	
	Olmesartan	✓	
	Telmisartan	✓	
	Valsartan	✓	
Antiaddictives	Naltrexone	!	⊗ Morphine
Anti-ADHD Agents	Amphetamine	!	⊗ Amoxapine
	Atomoxetine	!	
	Clonidine	✓	! Amoxapine
	Dextroamphetamine	!	⊗ Amoxapine
	Guanfacine	✓	
	Lisdexamfetamine	!	⊗ Amoxapine
Antianginal Agents	Ranolazine	!	
Antiarrhythmics	Flecainide	!	
	Mexiletine	!	
	Propafenone	!	

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CLASS	DRUG*	PHARMACOGENETIC RESULTS ✓	!	✗	INTERACTING DRUGS
Anticoagulants	*Apixaban*	✓			
	Betrixaban	✓			
	Dabigatran Etexilate	✓			
	Edoxaban	✓			
	Fondaparinux	✓			
	Rivaroxaban	✓			
	Warfarin	✓			
Anticonvulsants	Brivaracetam	✓			
	Carbamazepine	✓			! Morphine
	Eslicarbazepine	✓			
	Ethosuximide	✓			
	Ezogabine	✓			
	Felbamate	✓			
	Fosphenytoin	✓			! Morphine
	Gabapentin	✓			! Morphine
	Lacosamide	✓			
	Lamotrigine	✓			
	Levetiracetam	✓			
	Oxcarbazepine	✓			
	Perampanel	✓			
	Phenobarbital	✓			
	Phenytoin	✓			! Morphine
	Pregabalin	✓			! Morphine
	Primidone	✓			
	Rufinamide	✓			
	Tiagabine	✓			
	Topiramate	✓			
	Valproic Acid	✓			
	Vigabatrin	✓			
	Zonisamide	✓			
Antidementia Agents	Donepezil		!		
	Galantamine		!		
	Memantine	✓			

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CLASS	DRUG*	PHARMACOGENETIC RESULTS ✓	!	✗	INTERACTING DRUGS
	Amitriptyline			✗	
	Amoxapine		!		
	Citalopram			✗	
	Clomipramine			✗	
	Desipramine			✗	
	Desvenlafaxine	✓			! Amoxapine
	Doxepin			✗	
	Duloxetine		!		! Amoxapine
	Escitalopram			✗	
	Fluoxetine	✓			! Amoxapine
	Fluvoxamine		!		! Amoxapine
	Imipramine			✗	
Antidepressants	*Levomilnacipran*	✓			
	Maprotiline		!		
	Mirtazapine	✓			
	Nefazodone		!		
	Nortriptyline			✗	
	Paroxetine			✗	! Amoxapine
	Protriptyline			✗	
	Sertraline		!		! Amoxapine
	Trazodone	✓			
	Trimipramine			✗	
	Venlafaxine			✗	! Amoxapine
	Vilazodone	✓			
	Vortioxetine		!		

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CLASS	DRUG*	PHARMACOGENETIC RESULTS ✓	!	✗	INTERACTING DRUGS
Antiemetics	*Aprepitant*	✓			
	Dolasetron	✓			
	Dronabinol	✓			
	Fosaprepitant	✓			
	Granisetron		!		
	Metoclopramide		!		
	Netupitant-Palonosetron	✓			
	Ondansetron		!		
	Palonosetron	✓			
	Rolapitant	✓			
Antifungals	*Amphotericin B*	✓			
	Anidulafungin	✓			
	Caspofungin	✓			
	Fluconazole	✓			
	Isavuconazonium	✓			
	Itraconazole	✓			
	Micafungin	✓			
	Posaconazole	✓			
	Voriconazole			✗	
Anti-HIV Agents	*Dolutegravir*	✓			
	Raltegravir	✓			
Anti-Hyperuricemics and Anti-Gout Agents	*Colchicine*	✓			
	Febuxostat	✓			
	Lesinurad	✓			
Antimalarials	Proguanil	✓			
Antiplatelets	Clopidogrel		!		
	Prasugrel	✓			
	Ticagrelor	✓			
	Vorapaxar	✓			

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CLASS	DRUG*	PHARMACOGENETIC RESULTS			INTERACTING DRUGS
		✓	!	✗	
Antipsychotics	Aripiprazole		!		Morphine
	Asenapine	✓			
	Brexpiprazole		!		Morphine
	Cariprazine	✓			Morphine
	Chlorpromazine		!		Morphine
	Clozapine		!		Morphine
	Fluphenazine		!		Morphine
	Haloperidol			✗	Morphine
	Iloperidone		!		Morphine
	Loxapine	✓			Morphine
	Lurasidone	✓			Morphine
	Olanzapine		!		Morphine
	Paliperidone	✓			Morphine
	Perphenazine		!		Morphine
	Pimavanserin	✓			
	Pimozide		!		Amoxapine Morphine
	Quetiapine	✓			Morphine
	Risperidone			✗	Morphine
	Thioridazine			✗	Morphine
	Thiothixene	✓			Morphine
	Trifluoperazine	✓			Morphine
	Ziprasidone	✓			Morphine
Antispasmodics for Overactive Bladder	Darifenacin		!		
	Fesoterodine	✓			
	Mirabegron	✓			
	Oxybutynin	✓			
	Solifenacin	✓			
	Tolterodine		!		
	Trospium	✓			
Benzodiazepines	*Alprazolam*	✓			Morphine
	Clobazam	✓			Morphine
	Clonazepam	✓			Morphine
	Diazepam		!		Morphine

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CLASS	DRUG*	PHARMACOGENETIC RESULTS ✓	!	✗	INTERACTING DRUGS
Beta Blockers	*Atenolol*	✓			
	Bisoprolol	✓			
	Carvedilol		!		
	Labetalol	✓			
	Metoprolol			✗	
	Nebivolol	✓			
	Propranolol	✓			
	Timolol		!		
Cholinergic Agonists	Cevimeline		!		
Diuretics	Torsemide	✓			
Endocrine-Metabolic Agents	Eliglustat		!		
	Imiglucerase	✓			
	Miglustat	✓			
	Taliglucerase alfa	✓			
	Velaglucerase alfa	✓			
Fibromyalgia Agents	*Milnacipran*	✓			
Immunomodulators	*Apremilast*	✓			
	Leflunomide	✓			
	Tofacitinib	✓			
Immunosuppressants	Tacrolimus	✓			
Meglitinides	Nateglinide	✓			
	Repaglinide	✓			
Muscle Relaxants	Carisoprodol		!		! Morphine
	Cyclobenzaprine	✓			! Morphine
	Metaxalone	✓			! Morphine
	Methocarbamol	✓			! Morphine
	Tizanidine		!		! Morphine

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CLASS	DRUG*	PHARMACOGENETIC RESULTS	INTERACTING DRUGS
NSAIDs	Celecoxib	✓	
	Diclofenac	✓	
	Flurbiprofen	✓	
	Ibuprofen	✓	
	Indomethacin	✓	
	Ketoprofen	✓	
	Ketorolac	✓	
	Meloxicam	✓	
	Nabumetone	✓	
	Naproxen	✓	
	Piroxicam	✓	
	Sulindac	✓	
Opioids	*Alfentanil*	✓	
	Benzhydrocodone	!	
	Buprenorphine	✓	⊗ Morphine
	Codeine	✗	
	Dihydrocodeine	✓	
	Fentanyl	✓	
	Hydrocodone	!	
	Hydromorphone	✓	
	Levorphanol	✓	
	Meperidine	✓	
	Morphine	✓	
	Oxycodone	!	
	Oxymorphone	✓	
	Sufentanil	✓	
	Tapentadol	✓	⊗ Amoxapine
	Tramadol	✗	⊗ Amoxapine
Other Neurological Agents	Deutetrabenazine	!	
	Dextromethorphan / Quinidine	!	
	Flibanserin	✓	
	Tetrabenazine	!	
	Valbenazine	!	

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CLASS	DRUG*	PHARMACOGENETIC RESULTS ✓	!	✗	INTERACTING DRUGS
Phosphodiesterase Inhibitors for Erectile Dysfunction	*Avanafil*	✓			
	Sildenafil	✓			
	Tadalafil	✓			
	Vardenafil	✓			
Proton Pump Inhibitors	Dexlansoprazole		!		
	Esomeprazole		!		
	Lansoprazole		!		
	Omeprazole		!		
	Pantoprazole		!		
	Rabeprazole	✓			
Statins	Atorvastatin	✓			
	Fluvastatin	✓			
	Lovastatin	✓			
	Pitavastatin	✓			
	Pravastatin	✓			
	Rosuvastatin	✓			
	Simvastatin	✓			
Sulfonylureas	Chlorpropamide	✓			
	Glimepiride	✓			
	Glipizide	✓			
	Glyburide	✓			
	Tolbutamide	✓			

*Current patient medications are listed in bold whereas italicized drug names indicate drugs with no pharmacogenetic guidance

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3 Dosing Guidance

Amitriptyline

Increased Sensitivity to Amitriptyline (CYP2C19: Rapid Metabolizer) **INFORMATIVE**

Consider an alternative drug, or consider prescribing amitriptyline at standard dose and monitor the plasma concentrations of amitriptyline and nortriptyline to guide dose adjustments.

Citalopram

Insufficient Response to Citalopram (CYP2C19: Rapid Metabolizer) **ACTIONABLE**

At standard label-recommended dosage, citalopram plasma concentrations levels are expected to be low which may result in a loss of efficacy. Consider an alternative medication. If citalopram is warranted, consider increasing the dose to a maximum of 150% and titrate based on the clinical response and tolerability.

Clomipramine

Increased Sensitivity to Clomipramine (CYP2C19: Rapid Metabolizer) **INFORMATIVE**

Consider an alternative drug, or consider prescribing clomipramine at standard dose and monitor the plasma concentrations of clomipramine and desmethyl-clomipramine to guide dose adjustments.

Codeine

Non-Response to Codeine (CYP2D6: Poor Metabolizer) **ACTIONABLE**

Greatly reduced morphine levels are expected, and the patient may not experience adequate pain relief when taking codeine. Avoid prescribing codeine, and consider alternative opioids other than tramadol, or a non-opioid analgesic such as a NSAID or a COX-2 inhibitor. Unless contraindicated, available alternative opioids not sensitive to CYP2D6 function include: fentanyl, morphine, hydromorphone, oxymorphone, and tapentadol.

Desipramine

Increased Sensitivity to Desipramine (CYP2D6: Poor Metabolizer) **ACTIONABLE**

Consider an alternative drug, or prescribe desipramine at 50% of recommended standard starting dose. Monitor plasma concentrations of desipramine and metabolites and titrate accordingly until a favorable response is achieved.

Doxepin

Increased Sensitivity to Doxepin (CYP2C19: Rapid Metabolizer) **INFORMATIVE**

Consider an alternative drug, or consider prescribing doxepin at standard dose and monitor the plasma concentrations of doxepin and desmethyl-doxepin to guide dose adjustments.

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Escitalopram

Insufficient Reponse to Escitalopram (CYP2C19: Rapid Metabolizer) **ACTIONABLE**

At standard label-recommended dosage, escitalopram plasma concentrations levels are expected to be low which may result in a loss of efficacy. Consider an alternative medication. If escitalopram is warranted, consider increasing the dose to a maximum of 150% and titrate based on the clinical response and tolerability.

Haloperidol

Increased Sensitivity to Haloperidol (CYP2D6: Poor Metabolizer) **ACTIONABLE**

Haloperidol is metabolized by CYP2D6, CYP3A4, and other enzymes. **Decreased CYP2D6 activity results in higher haloperidol concentrations, potentially leading to more adverse events.** Consider an alternative drug, or prescribe haloperidol at 50% of the usual starting dose, then adjust dosage to achieve a favorable clinical response.

Imipramine

Increased Sensitivity to Imipramine (CYP2C19: Rapid Metabolizer) **INFORMATIVE**

Consider an alternative drug, or consider prescribing imipramine at the standard dose and monitor the plasma concentrations of imipramine and desipramine to guide dose adjustments.

Metoprolol

Significantly Increased Sensitivity to Metoprolol (CYP2D6: Poor Metabolizer) **ACTIONABLE**

Based on the genotype result, this patient is at risk of excessive beta-blockade when taking metoprolol at standard dosage. Heart Failure: Consider alternative beta-blockers such as bisoprolol or carvedilol, or prescribe metoprolol at a lower dose. When compared to a normal metabolizer, a poor metabolizer may require a 75% dose reduction. Other indications: Consider alternative beta-blockers such as bisoprolol or atenolol, or prescribe metoprolol at a lower dose. When compared to a normal metabolizer, a poor metabolizer may require a 75% dose reduction. If metoprolol is prescribed, be alert to adverse events (e.g., bradycardia or cold extremities).

Nortriptyline

Increased Sensitivity to Nortriptyline (CYP2D6: Poor Metabolizer) **ACTIONABLE**

Select an alternative drug, or consider prescribing nortriptyline at a reduced dose (50% reduction) with monitoring of plasma concentrations of nortriptyline and metabolites.

Paroxetine

Increased Sensitivity to Paroxetine (CYP2D6: Poor Metabolizer) **INFORMATIVE**

At standard label-recommended dosage, paroxetine levels are expected to be high, and adverse events may occur. Consider an alternative medication. If paroxetine is warranted, consider a 50% decrease of the initial dose and titrate based on the clinical response and tolerability. Some studies show that compared to normal metabolizers, poor metabolizers may experience more sexual dysfunction.

Protriptyline

Increased Sensitivity to Protriptyline (CYP2D6: Poor Metabolizer) **INFORMATIVE**

Consider alternative or prescribe protriptyline at 50% of recommended standard starting dose. Monitor plasma concentrations of protriptyline and metabolites and titrate accordingly until a favorable response is achieved.

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Risperidone

Significantly Increased Sensitivity to Risperidone (CYP2D6: Poor Metabolizer) **ACTIONABLE**

Consider an alternative drug, OR prescribe risperidone at a reduced dose, be extra alert of adverse events, and adjust dosage in response to clinical response and tolerability.

Thioridazine

Increased Sensitivity to Thioridazine (CYP2D6: Poor Metabolizer) **ACTIONABLE**

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.

Tramadol

Non-Response to Tramadol (CYP2D6: Poor Metabolizer) **ACTIONABLE**

The patient will not experience adequate pain relief when taking tramadol. Avoid prescribing tramadol, and consider alternative opioids other than codeine or a non-opioid analgesic such as a NSAID or a COX-2 inhibitor. Unless contraindicated, available alternative opioids not sensitive to CYP2D6 function include: fentanyl, morphine, hydromorphone, oxymorphone, and tapentadol.

Trimipramine

Increased Sensitivity to Trimipramine (CYP2C19: Rapid Metabolizer) **INFORMATIVE**

Consider an alternative drug, or consider prescribing trimipramine at standard dose and monitor the plasma concentrations of trimipramine and desmethyl-trimipramine to guide dose adjustments.

Venlafaxine

Significantly Increased Sensitivity to Venlafaxine (CYP2D6: Poor Metabolizer) **ACTIONABLE**

The patient has an increased risk of side effects when taking standard doses of venlafaxine. Consider an alternative drug, OR prescribe venlafaxine, be extra alert of adverse events, and adjust dosage in response to clinical response and tolerability. Monitor O-desmethylvenlafaxine plasma concentrations.

Voriconazole

Non-Response to Voriconazole (CYP2C19: Rapid Metabolizer) **ACTIONABLE**

Voriconazole plasma concentrations are expected to be low if a standard dose is used, increasing the risk of loss of response and effectiveness and subsequent disease progression. Consider an alternative medication that is not dependent on CYP2C19 metabolism, such as isavuconazole, liposomal amphotericin B or posaconazole.

Amoxapine

Possible Sensitivity to Amoxapine (CYP2D6: Poor Metabolizer) **INFORMATIVE**

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.

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Amphetamine

Possible Increased Exposure to Amphetamine (CYP2D6: Poor Metabolizer) — INFORMATIVE

There is little evidence documenting the exposure of amphetamine in subjects with reduced CYP2D6 activity such as CYP2D6 poor metabolizers. Although the drug's plasma concentrations may be elevated in these subjects, the clinical relevance of this change is not well documented. Consider initiating therapy with lower doses and monitor the patient more frequently during drug titration. Consider adjusting the dose based on clinical response and tolerability. An alternative therapy may also be considered in patients with decreased tolerability.

Aripiprazole

Increased Sensitivity to Aripiprazole (CYP2D6: Poor Metabolizer) — ACTIONABLE

CYP2D6 poor metabolizers have a significantly reduced capacity to metabolize aripiprazole and its active metabolite, and should receive lower doses. Careful titration is recommended until a favorable response is achieved.

Daily dosing (oral or intramuscular): aripiprazole dose should initially be reduced to one-half (**50%**) of the usual dose, then adjusted to achieve a favorable clinical response. Reduce the **maximum dose to 10 mg/day** (67% of the maximum recommended daily dose). The dose of aripiprazole for CYP2D6 poor metabolizers who are administered a strong CYP3A4 inhibitor should be reduced to one-quarter (25%) of the usual dose.

Monthly dosing (intramuscular): for *Abilify Maintena*, the starting and maintenance monthly recommended dose is lower than the usually recommended dose, and should be **300 mg**. Some patients may benefit from a reduction to 200 mg. For *Aristada*, reduce the dose to the next lower strength (662 mg instead of 882 mg and 441 mg instead of 662 mg); no dosage adjustment is necessary in patients taking 441 mg *Aristada*, if tolerated. For *Abilify Maintena*, reduce the monthly dose to 200 mg if a CYP3A4 inhibitor is prescribed to CYP2D6 poor metabolizers receiving 300 mg of aripiprazole. For *Aristada*, reduce dose to 441 mg and avoid use at 662 mg or 882 mg dose if a CYP3A4 inhibitor is prescribed to CYP2D6 poor metabolizers for more than 14 days. No dosage adjustment is necessary in patients taking 441 mg *Aristada*, if tolerated.

Every 6 weeks or two months dosing with *Aristada* (intramuscular): reduce the dose to a lower strength of 441 mg every 4 weeks. If a strong CYP3A4 inhibitor is coadministered for more than 14 days, avoid using the 662 mg, 882 mg or 1064 mg doses and consider the lower dose strenght of 441 mg every 4 weeks.

Atomoxetine

Increased Sensitivity to Atomoxetine (CYP2D6: Poor Metabolizer) — ACTIONABLE

When given a standard atomoxetine dose, CYP2D6 poor metabolizers are likely to have higher plasma levels of the drug, which may lead to a higher rate of adverse events. **Careful titration and dosing adjustment are recommended with monitoring for toxicity until a favorable response is achieved**. In children and adolescents up to 70 kg body weight, atomoxetine should be initiated at standard dosing of 0.5 mg/kg/day, and only increased to the usual target dose of 1.2 mg/kg/day if symptoms fail to improve after 4 weeks and the initial dose is well tolerated. In children and adolescents over 70 kg body weight and adults, atomoxetine should be initiated at standard dosing of 40 mg/day, and only increased to the usual target dose of 80 mg/day if symptoms fail to improve after 4 weeks and the initial dose is well tolerated.

Benzhydrocodone

Possible Altered Response to Benzhydrocodone (CYP2D6: Poor Metabolizer) — INFORMATIVE

Benzhydrocodone is a prodrug of hydrocodone and is converted to active hydrocodone by intestinal enzymes. Decreased conversion of hydrocodone to the more active metabolite hydromorphone is expected in CYP2D6 poor metabolizers. However, there is insufficient evidence whether these patients have decreased analgesia when taking benzhydrocodone. Adequate pain relief can be achieved by increasing the dose in response to pain symptoms. Other opioids not metabolized by CYP2D6 may also be considered (i.e., morphine, oxymorphone, buprenorphine, fentanyl, methadone, and hydromorphone).

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Brexpiprazole

Increased Sensitivity to Brexpiprazole (CYP2D6: Poor Metabolizer) **ACTIONABLE**

The exposure to brexpiprazole in CYP2D6 poor metabolizers is 120% higher than the exposure in CYP2D6 normal metabolizers. Because the incidence of akathisia is dose-related in patients suffering from schizophrenia or major depressive disorders, **it is recommended to prescribe half of the usual doses of brexpiprazole to CYP2D6 poor metabolizers.** Careful titration is recommended until a favorable response is achieved.

Adjunctive Treatment of Major Depression Disorder: the recommended starting doses should be reduced by half (0.25 mg or 0.5 mg once daily). The daily maintenance doses and maximum recommended dose are 0.5-1 mg and 1.5 mg, respectively. Schizophrenia: the recommended starting dose is 0.5 mg once daily. The daily maintenance doses and maximum recommended dose are 1-2 mg and 2 mg, respectively.

Dose adjustments with comedications: Administer **a quarter of the usual dose** if a strong/moderate CYP3A4 inhibitor is coadministered. Double usual dose over 1 to 2 weeks if a strong CYP3A4 inducer is coadministered.

Carisoprodol

Altered Sensitivity to Carisoprodol (CYP2C19: Rapid Metabolizer) **INFORMATIVE**

There is insufficient data to allow calculation of dose adjustment. If carisoprodol is prescribed, it is recommended to use a lower dose, and to carefully monitor the patient for side effects.

Carvedilol

Moderate Sensitivity to Carvedilol (CYP2D6: Poor Metabolizer) **ACTIONABLE**

CYP2D6 poor metabolizers may experience dizziness during up-titration. Carvedilol can be prescribed at standard label-recommended dosage and administration. Careful titration is recommended with monitoring until a favorable response is achieved.

Cevimeline

Increased Sensitivity to Cevimeline (CYP2D6: Poor Metabolizer) **ACTIONABLE**

Cevimeline is metabolized by CYP2D6. However, the overall contribution of this enzyme in the metabolism of this drug is not well documented. Lack of CYP2D6 activity may result in higher cevimeline concentrations potentially leading to higher adverse events. There are no established dosing adjustments for CYP2D6 poor metabolizers therefore, cevimeline must be initiated cautiously and dosing may be adjusted according to the patient's response.

Chlorpromazine

Increased Sensitivity to Chlorpromazine (CYP2D6: Poor Metabolizer) **INFORMATIVE**

Chlorpromazine is metabolized by CYP2D6, CYP3A4 and flavin-containing monooxygenases. Decreased CYP2D6 activity results in higher chlorpromazine concentrations potentially leading to higher adverse events. Consider prescribing chlorpromazine at a lower starting dose and then adjust dosage to achieve a favorable clinical response.

Clopidogrel

Increased Response to Clopidogrel (CYP2C19: Rapid Metabolizer) **ACTIONABLE**

Clopidogrel can be prescribed at standard label-recommended dosage. Individuals with the *17 allele may have an increased risk of bleeding while taking clopidogrel.

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Clozapine

Non-Response to Clozapine (CYP1A2: Normal Metabolizer - Higher Inducibility) **INFORMATIVE**

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.

Darifenacin

Possible Sensitivity to Darifenacin (CYP2D6: Poor Metabolizer) **ACTIONABLE**

Darifenacin exposure is increased up-to 2.6-fold in CYP2D6 poor metabolizers. Although dose adjustment may not be needed in these patients, monitor patients for increased side effects when darifenacin is prescribed at standard label-recommended dosage and administration.

Deutetrabenazine

Increased Sensitivity to Deutetrabenazine (CYP2D6: Poor Metabolizer) **ACTIONABLE**

For treating chorea associated with Huntington's disease: The exposure to deutetrabenazine active metabolites alpha- and and beta-dihydrotetrabenazine is expected to be increased in CYP2D6 poor metabolizers (approximately 3-fold compared to CYP2D6 normal metabolizers) and clinically relevant QT prolongation might be expected in some patients at highest therapeutic doses. Therefore, the maximum recommended dosage of deutetrabenazine in CYP2D6 poor metabolizers is 36 mg per day. Individualization of dose with careful weekly titration is required. The first week's starting dose is 6 mg once daily then this dose should be slowly titrated at weekly intervals by 6 mg per day based on tolerability and up to a maximum recommended daily dosage of 36 mg (18 mg twice daily).

Dexlansoprazole

Insufficient Response to Dexlansoprazole (CYP2C19: Rapid Metabolizer) **INFORMATIVE**

Dexlansoprazole is the R-enantiomer of lansoprazole.

- Helicobacter pylori eradication: increase dose by 200% and be alert to insufficient response.
- Other: be extra alert to insufficient response and consider dose increase of 200%.

Dextroamphetamine

Possible Increased Exposure to Dextroamphetamine (CYP2D6: Poor Metabolizer) **INFORMATIVE**

There is little evidence documenting the exposure of dextroamphetamine in subjects with reduced CYP2D6 activity such as CYP2D6 poor metabolizers. Although the drug's plasma concentrations may be elevated in these subjects, the clinical relevance of this change is not well documented. Consider initiating therapy with lower doses and monitor the patient more frequently during drug titration. Consider adjusting the dose based on clinical response and tolerability. An alternative therapy may also be considered in patients with decreased tolerability.

Dextromethorphan / Quinidine

Altered Sensitivity to Dextromethorphan-Quinidine (CYP2D6: Poor Metabolizer) **ACTIONABLE**

Patients with Pseudobulbar Affect: the quinidine component of dextromethorphan-quinidine is intended to inhibit CYP2D6 so that higher exposure to dextromethorphan can be achieved compared to when dextromethorphan is given alone. Quinidine does not further inhibit CYP2D6 metabolism in poor metabolizers (PMs) and this component may expose PMs to an unnecessary risk since quinidine is not adding any benefit. Prescribers should consider the potential risk for quinidine-related adverse events relative to the benefit of administering the dextromethorphan-quinidine combination product (vs. dextromethorphan alone) in known CYP2D6 poor metabolizers.

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Diazepam

Possible Altered Sensitivity to Diazepam (CYP2C19: Rapid Metabolizer) **INFORMATIVE**

CYP2C19 rapid and ultra-rapid metabolizers metabolize diazepam and nordiazepam more rapidly than normal metabolizers. However, there is insufficient data to allow calculation of dose adjustment when diazepam is prescribed. Monitor the patient's response and adjust the dose accordingly.

Donepezil

Possible Altered Response to Donepezil (CYP2D6: Poor Metabolizer) **INFORMATIVE**

When compared to a normal metabolizer, a poor metabolizer has a 30% decrease in donepezil clearance. The clinical significance of this decrease is not well documented. Consider using a standard dosing regimen, be alert for adverse events, and adjust dosage in response to clinical response and tolerability.

Duloxetine

Possible Sensitivity to Duloxetine (CYP2D6: Poor Metabolizer) **INFORMATIVE**

Limited data suggest that duloxetine plasma concentrations might be increased in CYP2D6 poor metabolizers. Therefore, duloxetine can be prescribed at standard label-recommended dosage, and careful titration is recommended until a favorable response is achieved.

Eliglustat

Increased Sensitivity to Eliglustat (CYP2D6: Poor Metabolizer) **ACTIONABLE**

Eliglustat plasma concentrations are expected to be high in CYP2D6 poor metabolizers, which may increase the risk of dose-dependent adverse events. Consider prescribing eliglustat at half the recommended dose: 84 mg orally once daily. Appropriate adverse events monitoring is recommended.

Dose adjustments with comedications: Co-administration of eliglustat with drugs that inhibit CYP2D6 and CYP3A may significantly increase the exposure to eliglustat and result in prolongation of the PR, QTc, and/or QRS cardiac interval, which could result in cardiac arrhythmias. Eliglustat is not recommended if a moderate/weak CYP3A inhibitor is co-administered. Eliglustat is contraindicated if a strong CYP3A inhibitor is co-administered or a strong/moderate CYP2D6 inhibitor AND a strong CYP3A inhibitor are co-administered.

Esomeprazole

Insufficient Response to Esomeprazole (CYP2C19: Rapid Metabolizer) **INFORMATIVE**

- Helicobacter pylori eradication: increase dose by 50-100% and be alert to insufficient response.
- Other: be extra alert to insufficient response and consider dose increase of 50-100%.

Flecainide

Significantly Increased Sensitivity to Flecainide (CYP2D6: Poor Metabolizer) **ACTIONABLE**

Consider prescribing a lower flecainide dose. When compared to a CYP2D6 normal metabolizer, a poor metabolizer may require a 50% dose reduction. Careful titration with ECG recording and monitoring of flecainide plasma concentrations are recommended until a favorable clinical response is achieved.

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Fluphenazine

Increased Sensitivity to Fluphenazine (CYP2D6: Poor Metabolizer) **INFORMATIVE**

Fluphenazine is metabolized by CYP2D6, CYP1A2 and other enzymes. **Decreased CYP2D6 activity may result in higher fluphenazine concentrations potentially leading to higher adverse events such as extrapyramidal symptoms**. There are no established dosing adjustments for patients lacking CYP2D6 function therefore, therapy must be initiated cautiously with oral or parenteral fluphenazine hydrochloride. When the pharmacological effects and an appropriate dosage are apparent, an equivalent dose of fluphenazine decanoate (IM or SC) may be administered and subsequent dosage adjustments may be necessary.

Fluvoxamine

Increased Sensitivity to Fluvoxamine (CYP2D6: Poor Metabolizer) **INFORMATIVE**

At standard label-recommended dosage, fluvoxamine levels are expected to be high and adverse events may occur. Consider a 25-50% reduction of recommended starting dose to help prevent concentration-dependent adverse events and titrate based on the clinical response and tolerability. An alternative medication may also be considered.

Galantamine

Possible Sensitivity to Galantamine (CYP2D6: Poor Metabolizer) **INFORMATIVE**

A CYP2D6 poor metabolizer has a drug exposure that is approximately 50% higher than the exposure in a normal metabolizer. Although dosage adjustment is not necessary in a patient identified as a CYP2D6 poor metabolizer as the dose of drug is individually titrated to tolerability, a slower titration can be considered as it may improve tolerability.

Granisetron

Unfavorable Response to Standard Granisetron Dosing (ABCB1: Heterozygous- Variant Allele Present) **INFORMATIVE**

The genotype result predicts that the patient has high ABCB1 transporter expression. An increased risk of vomiting has been reported in patients with high ABCB1 transporter expression when taking standard doses of granisetron. Monitor for decreased response.

Hydrocodone

Possible Altered Response to Hydrocodone (CYP2D6: Poor Metabolizer) **INFORMATIVE**

Decreased conversion of hydrocodone to the more active metabolite hydromorphone is expected in CYP2D6 poor metabolizers. However, there is insufficient evidence whether poor metabolizers have decreased analgesia when taking hydrocodone. Adequate pain relief can be achieved by increasing the dose in response to pain symptoms. Other opioids not metabolized by CYP2D6 may also be considered (i.e., morphine, oxymorphone, buprenorphine, fentanyl, methadone, and hydromorphone).

Iloperidone

Increased Sensitivity to Iloperidone (CYP2D6: Poor Metabolizer) **ACTIONABLE**

Iloperidone **dose should be reduced by one-half and titrated slowly to avoid orthostatic hypotension**. Because iloperidone is associated with QTc prolongation, caution is warranted when prescribing the drug in patients with reduced CYP2D6 activity. 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.

Lansoprazole

Insufficient Response to Lansoprazole (CYP2C19: Rapid Metabolizer) **INFORMATIVE**

- Helicobacter pylori eradication: increase dose by 200% and be alert to insufficient response.
- Other: be extra alert to insufficient response and consider dose increase of 200%.

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Lisdexamfetamine

Possible Increased Exposure to Lisdexamfetamine Active Metabolite (CYP2D6: Poor Metabolizer) **INFORMATIVE**

There is little evidence documenting the exposure of lisdexamfetamine and its active metabolite dextroamphetamine in subjects with reduced CYP2D6 activity such as CYP2D6 poor metabolizers. Although dextroamphetamine plasma concentrations may be elevated in these subjects, the clinical relevance of this change is not well documented. Consider initiating therapy with lower doses and monitor the patient more frequently during drug titration. Consider adjusting the dose based on clinical response and tolerability. An alternative therapy may also be considered in patients with decreased tolerability.

Maprotiline

Increased Sensitivity to Maprotiline (CYP2D6: Poor Metabolizer) **INFORMATIVE**

Like other tricyclic and tetracyclic antidepressants, maprotiline is metabolized by CYP2D6 as well as CYP1A2. Compared to CYP2D6 normal metabolizers, CYP2D6 poor metabolizers have higher exposure to maprotiline at therapeutic doses which may increase the risk of concentration-dependent toxicities. There are no established dosing adjustments for patients with decreased CYP2D6 function however, it is recommended to initiate maprotiline therapy at a low dosage and gradually adjust the dosing according to the patient's response. The lowest effective dosage should always be considered during maintenance therapy.

Metoclopramide

Increased Sensitivity to Metoclopramide (CYP2D6: Poor Metabolizer) **ACTIONABLE**

Metoclopramide is metabolized at a slower rate in CYP2D6 poor metabolizers. Slower metabolism results in significantly higher metoclopramide serum concentrations and increased risk of CNS and extrapyramidal adverse effects. Consider reducing the dose to 5 mg four times a day or 10 mg three times a day. The maximum recommended daily dose should not exceed 30 mg in these patients.

Mexiletine

Significantly Increased Sensitivity to Mexiletine (CYP2D6: Poor Metabolizer) **ACTIONABLE**

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.

Naltrexone

Altered Response to Naltrexone (OPRM1: Normal OPRM1 Function) **INFORMATIVE**

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.

Nefazodone

Possible Sensitivity to Nefazodone (CYP2D6: Poor Metabolizer) **INFORMATIVE**

Nefazodone is metabolized by CYP3A4 to its active metabolite m-chlorophenylpiperazine and other metabolites. The m-chlorophenylpiperazine metabolite which may contribute to adverse events, is further metabolized by CYP2D6. Individuals lacking CYP2D6 activity have higher levels of m-chlorophenylpiperazine metabolite and may experience more moderate and transient side effects when starting therapy. Consider prescribing nefazodone at a lower dose and adjust dose according to the patient's tolerability and clinical response.

Olanzapine

Non-Response to Olanzapine (CYP1A2: Normal Metabolizer - Higher Inducibility) **INFORMATIVE**

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.

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Omeprazole

Insufficient Response to Omeprazole (CYP2C19: Rapid Metabolizer) **ACTIONABLE**

- Helicobacter pylori eradication: increase dose by 100-200% and be alert to insufficient response.
- Other: be extra alert to insufficient response and consider dose increase of 100-200%.

Ondansetron

Unfavorable Response to Standard Ondansetron Dosing (ABCB1: Heterozygous- Variant Allele Present) **INFORMATIVE**

The genotype result predicts that the patient has high ABCB1 transporter expression. An increased risk of vomiting has been reported in patients with high ABCB1 transporter expression when taking standard doses of ondansetron. Monitor for decreased response.

Oxycodone

Possible Altered Response to Oxycodone (CYP2D6: Poor Metabolizer) **ACTIONABLE**

Decreased conversion of oxycodone to the more active metabolite oxymorphone is expected in CYP2D6 poor metabolizers. However, there is insufficient evidence whether poor metabolizers have decreased analgesia when taking oxycodone. Adequate pain relief can be achieved by increasing the dose in response to pain symptoms. Other opioids not metabolized by CYP2D6 may also be considered (i.e., morphine, oxymorphone, buprenorphine, fentanyl, methadone, and hydromorphone).

Pantoprazole

Insufficient Response to Pantoprazole (CYP2C19: Rapid Metabolizer) **ACTIONABLE**

- Helicobacter pylori eradication: increase dose by 400% and be alert to insufficient response.
- Other: be extra alert to insufficient response and consider dose increase of 400%.

Perphenazine

Increased Sensitivity to Perphenazine (CYP2D6: Poor Metabolizer) **ACTIONABLE**

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.

Pimozide

Increased Sensitivity to Pimozide (CYP2D6: Poor Metabolizer) **ACTIONABLE**

The pimozide concentrations observed in poor CYP2D6 metabolizers are expected to be high, and the time to achieve steady-state pimozide concentrations is expected to be long (approximately 2 weeks). Consequently, CYP2D6 poor metabolizers are at an increased risk of QT prolongation at standard doses of pimozide. In CYP2D6 poor metabolizers, pimozide doses should not exceed 4 mg/day in adults or 0.05 mg/kg/day in children, and doses should not be increased earlier than 14 days.

Propafenone

Increased Sensitivity to Propafenone (CYP2D6: Poor Metabolizer) **ACTIONABLE**

Consider reducing propafenone initial dose, and monitor ECG and plasma concentrations. Compared to normal metabolizers, poor metabolizers may require a 70% dose reduction of the initial dose.

Dose adjustments with comedications: increased exposure to propafenone may lead to cardiac arrhythmias and exaggerated beta-adrenergic blocking activity. Concurrent use of propafenone along with CYP3A4 inhibitors and CYP2D6 inhibitors may significantly increase the plasma concentration of propafenone and thereby increase the risk of proarrhythmia and other adverse events. Therefore, avoid simultaneous use of propafenone with a CYP3A4 inhibitor.

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Ranolazine

Increased Sensitivity to Ranolazine (CYP2D6: Poor Metabolizer) **ACTIONABLE**

Ranolazine is metabolized mainly by CYP3A4, and to a lesser extent by CYP2D6. At 500 mg twice daily, subjects lacking CYP2D6 activity (poor metabolizers) had 62% higher ranolazine exposure than subjects with normal CYP2D6 activity. The corresponding difference at 1000 mg twice daily dose was 25%.

The risk for increased exposure leading to adverse events is higher in patients lacking CYP2D6 activity (i.e., poor metabolizers). The recommended initial oral dose is 375 mg twice daily. **A slower up titration and additional monitoring is recommended in these patients.** Exposure related side effects might include nausea, vomiting, syncope, and dizziness. If a patient experiences treatment-related adverse events, down titration of the dose to 500 mg or 375 mg twice daily may be required. If symptoms do not resolve after dose reduction, treatment should be discontinued.

Ranolazine is a QTc prolonging drug. Caution should be observed when treating: 1- patients with a history of congenital or a family history of long QT syndrome, 2- patients with known acquired QT interval prolongation, and 3- patients treated with drugs affecting the QTc interval. Administration of CYP3A4 inhibitors increases the exposure of ranolazine significantly. As a consequence, the QTc prolongation by ranolazine in the presence of potent CYP3A inhibitors is significantly elevated relative to when the drug is administered alone.

Sertraline

Possible Reduced Response to Sertraline (CYP2C19: Rapid Metabolizer) **INFORMATIVE**

Sertraline can be prescribed at standard label-recommended dosage and administration. If patient does not respond to recommended maintenance dosing, consider an alternative medication.

Tamsulosin

Increased Sensitivity to Tamsulosin (CYP2D6: Poor Metabolizer) **ACTIONABLE**

Tamsulosin is metabolized at a slower rate in CYP2D6 poor metabolizers, which results in significantly higher serum concentrations of tamsulosin. Therefore, this drug should be used with caution in patients known to be CYP2D6 poor metabolizers, particularly at a daily dose higher than 0.4 mg.

Tetrabenazine

Increased Sensitivity to Tetrabenazine (CYP2D6: Poor Metabolizer) **ACTIONABLE**

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 poor metabolizers is 50 mg with a maximum single dose of 25 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.

Timolol

Increased Sensitivity to Timolol (CYP2D6: Poor Metabolizer) **ACTIONABLE**

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.

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Tizanidine

Possible Non-Response to Tizanidine (CYP1A2: Normal Metabolizer - Higher Inducibility) **INFORMATIVE**

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.

Tolterodine

Possible Sensitivity to Tolterodine (CYP2D6: Poor Metabolizer) **INFORMATIVE**

Tolterodine is metabolized at a slower rate in CYP2D6 poor metabolizers, which results in significantly higher serum concentrations of tolterodine and negligible concentrations of its active metabolite (5-hydroxymethytolterodine). Considering the antimuscarinic potency of tolterodine and its active metabolite, and the protein binding of these compounds, tolterodine accounts for the major part of the clinical effect in poor metabolizers, and the same dosage can be applied irrespective of phenotype status.

Patients with congenital or acquired QT prolongation: the effect of tolterodine on the QT interval prolongation is greater for 8 mg/day (two times the therapeutic dose) compared to 4 mg/day, and is more pronounced in CYP2D6 poor metabolizers than normal metabolizers. This should be considered when tolterodine is prescribed to patients with a known history of QT prolongation, or patients who are taking Class IA or Class III antiarrhythmics.

Valbenazine

Increased Sensitivity to Valbenazine (CYP2D6: Poor Metabolizer) **ACTIONABLE**

The initial dose is 40 mg once daily. Based on tolerability, this dose may be maintained in CYP2D6 poor metabolizers to reduce the risk of exposure-related adverse events. Valbenazine may prolong the QT interval. The exposure to valbenazine and its major active metabolite in CYP2D6 poor metabolizers is significantly higher than the exposure in CYP2D6 normal metabolizers. Because the drug's QTc prolongation effect is concentration-dependent, it is appropriate to consider a reduced recommended dose based on the patient's tolerability. Other exposure-related adverse events include somnolence. Careful titration is recommended until a favorable response is achieved.

Dose adjustments with comedications: reduce the daily recommended dose to 40 mg if a strong CYP3A4 inhibitor is coadministered. Concomitant use with CYP3A4 inducers should be avoided.

Vortioxetine

Increased Sensitivity to Vortioxetine (CYP2D6: Poor Metabolizer) **ACTIONABLE**

CYP2D6 is the primary enzyme catalyzing the metabolism of vortioxetine to its major, pharmacologically inactive carboxylic acid metabolite. CYP2D6 poor metabolizers have approximately twice the vortioxetine plasma concentrations of normal metabolizers. **Vortioxetine starting dose should be reduced by one-half. The maximum recommended dose is 10 mg/day in known CYP2D6 poor metabolizers.** Consider 5 mg/day for patients who do not tolerate higher doses.

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4 Test details

GENE	GENOTYPE	PHENOTYPE	ALLELES TESTED
CYP2D6	*3/*5	Poor Metabolizer	*2, *3, *4, *4M, *6, *7, *8, *9, *10, *11, *12, *14A, *14B, *15, *17, *18, *19, *20, *29, *41, *5 (gene deletion), XN (gene duplication)
CYP2C19	*1/*17	Rapid Metabolizer	*2, *3, *4, *4B, *5, *6, *7, *8, *17
CYP1A2	*1A/*1F	Normal Metabolizer - Higher Inducibility	*1C, *1F, *1K, *1L, *7, *11
CYP3A4	*1/*1	Normal Metabolizer	*2, *17, *22
CYP3A5	*3/*3	Poor Metabolizer	*2, *3, *3C, *6, *7
CYP2C9	*1/*1	Normal Metabolizer	*2, *3, *4, *5, *6, *8, *11, *12, *13, *15, *25, *27
VKORC1	-1639G>A G/G	Low Warfarin Sensitivity	-1639G>A
ABCB1	3435C>T C/T	Heterozygous- Variant Allele Present	3435C>T
OPRM1	A118G A/A	Normal OPRM1 Function	A118G
SLCO1B1	521T>C T/T	Normal Function	521T>C

Lab disclaimer

Genotyping is performed at Douglass Hanly Moir Pathology, a NATA accredited laboratory and member of the Sonic Healthcare Group, using the iPLEX® PGx 74 panel and MassARRAY® System (Agena Bioscience). CYP2D6 copy number is determined using a TaqMan real-time PCR specific for exon 9 (Applied Biosystems). The allele affected by increased copy number is not determined by this assay. These methods will not detect all known variants that result in altered or no activity of the genes tested. Individuals without detectable gene variants may still experience altered drug response due to other genetic and non-genetic factors.

Allele assignment and genotype-phenotype associations are provided by Translational Software (www.translationalsoftware.com). The accuracy of this information may change with advances in pharmacogenomic knowledge and technology.

Translational Software disclaimer

The information presented on this report is provided as general educational health information. The content is not intended to be a substitute for professional medical advice, diagnosis, or treatment. Only a physician, pharmacist or other healthcare professional should advise a patient on the use of the medications prescribed.

The pharmacogenetic assay involves use of reporting software and genotype-phenotype associations performed by Translational Software (www.translationalsoftware.com). The software has not been evaluated by the Food and Drug Administration. The software, and the report generated by the software, is not intended to diagnose, treat, cure, or prevent any disease. A qualified designee within the lab uses Translational Software to generate and subsequently review the report. The pharmacogenetic report is one of multiple pieces of information that clinicians should consider in guiding their therapeutic choice for each patient. It remains the responsibility of the health-care provider to determine the best course of treatment for a patient. Adherence to dose guidelines does not necessarily assure a successful medical outcome.

Drug interaction data is provided by First Databank (FDB) and FDB is entirely responsible for its accuracy. The drug interaction report is solely intended to be used by a medical professional. The drug interaction report is based on patient-reported medications and does not account for other factors, such as smoking history, tobacco use, diet and other underlying chronic conditions such as diabetes or heart disease. Unreported medications, herbal medications, over-the-counter supplements and other non- FDA-approved medications are not considered in the drug interaction report, but may cause drug interactions. The treating medical professional bears the ultimate responsibility for all treatment decisions made in regards to the patient, including any decisions based on the drug interaction report.

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