Sonic Genetics
Douglass Hanly Moir Pathology

Sample Patient

LAB ID **987654321** DOB **23/07/1979** (**39Y Female**)
Referring Doctor Dr Kate Goodhealth
Your ref. 987654321
Address Goodhealth Medical Clinic
Phone

Requested 16 Aug 2019
Collected 16 Aug 2019 06:00 am
Received 16 Aug 2019 14:30 pm
Reported 26 Sep 2019 06:40 am

Dr Kate Goodhealth
Goodhealth Medical Clinic
123 Address Road
SUBURBTOWN NSW 2000

Sonic PGx Panel

Pharmacogenomic Report

Interpreting this report

This report is divided into four sections for easy navigation.

1. Specified patient medications
2. Potentially impacted medications (and alternatives)
3. Dosing guidance
4. Test details - genotype results

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

EXAMPLE

Clinical notes

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Results (02) 9855 5100
Pathologists (02) 9855 5150 | All Hours (02) 9855 5222 | Toll Free 1800 222 365
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Sonic PGx Panel

Pharmacogenomic Report

1 PGx review of specified medications

Escitalopram

Insufficient Response 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.

Venlafaxine

Non-Response to Venlafaxine (CYP2D6: Ultra-Rapid Metabolizer) — ACTIONABLE

The patient is unlikely to achieve adequate serum levels of venlafaxine and O-desmethylvenlafaxine when taking standard doses of venlafaxine. Consider an alternative drug, or increase the venlafaxine dose to a maximum of 150% of the normal dose and monitor venlafaxine and O-desmethylvenlafaxine plasma concentrations.

Lamotrigine

Normal Response to Lamotrigine — INFORMATIVE

Pharmacogenetic guidance: Genotype results obtained from the pharmacogenetic test performed in this patient cannot be used to identify patients at risk for severe cutaneous adverse reactions such as anticonvulsant hypersensitivity syndrome, Stevens-Johnson syndrome (SJS) and toxic epidermal necrolysis (TEN). Lamotrigine is metabolized by glucuronidation, which is mediated primarily by UGT1A4 with some contribution from UGT1A1 and UGBT2B7. There are insufficient studies documenting the impact of genetic polymorphisms of these metabolizing enzymes on lamotrigine response. No genetically guided drug selection or dosing recommendations are available. Polypharmacy guidance: Enzyme-inducing drugs increase lamotrigine clearance significantly, and higher doses of this drug are required to maintain therapeutic concentrations. Coadministration of valproic acid, an inhibitor of UGT enzymes, increases lamotrigine levels and may result in serious lamotrigine adverse effects (neurological and cutaneous). A low starting dose with a slow titration schedule is recommended when lamotrigine is added to existing valproic acid treatment.

Quetiapine

Normal Response to Quetiapine — INFORMATIVE

Pharmacogenetic guidance: Quetiapine is predominantly metabolized to several metabolites by CYP3A4. CYP3A5 and CYP2D6 are also responsible for quetiapine metabolism but their role in the overall metabolism of this drug is minor compared to CYP3A4. N-desalkylquetiapine, a pharmacologically active metabolite (responsible of the antidepressant effect) is further metabolized by CYP2D6 and CYP3A4. Preliminary studies have shown that genetic polymorphisms of CYP3A4, CYP2D6 and CYP3A5 enzymes may be responsible in variable exposures to quetiapine and to its active metabolite N-desalkylquetiapine. However, the clinical significance of these changes is not established yet and no genetically guided drug selection or dosing recommendations are available. Quetiapine dose should be titrated based on the clinical response and tolerability of the individual patient. Polypharmacy guidance: Quetiapine dose should be reduced to one sixth of original dose when co-medicated with a potent CYP3A4 inhibitor (e.g., ketoconazole, itraconazole, indinavir, ritonavir, nefazodone). When the CYP3A4 inhibitor is discontinued, the dose should be increased by 6 fold. Quetiapine dose should be increased up to 5 fold of the original dose when used in combination with a chronic treatment (e.g. > 7-14 days) of a potent CYP3A4 inducer (e.g., phenytoin, carbamazepine, rifampin, St. John's wort etc.). When the CYP3A4 inducer is discontinued, the dose should be reduced to the original level within 7-14 days.

EXAMPLE

Unrecognised Medications *: None
Medications outside the scope of the report #: Lithium

Legend

Prescribing guidance

- Medication should not be prescribed due to potentially reduced efficacy or increased toxicity.
- Medication can be prescibed with dose adjustment and/or with increased monitoring.
- Medication can be prescribed according to standard dosing guidelines with standard monitoring of medication effects.

Evidence levels for prescribing guidance

ACTIONABLE	Recommendations are suitable for Implementation in a clincial setting. Recommendations extracted from evidence based guidelines issued by international pharmacogenetic consortia, proffessional societies or regulatory bodies (CPIC, DPWG, FDA, EMA, CPNDS, 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.

Note:
***Unrecognised medications** include medications that are not included in the testing database; medications that were misspelled on the Sonic PGx request form, medications that were listed as drug classes instead of individual medications, and/or medications not available in Australia. Please note: some medications use the US spellings.
#Out-of-scope medications are those that do not have PGx guidance to report.

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2 Potential suitability of other medications

Legend

Bold type indicates medications referred to in section 1

^ Indicates medications for which there is no PGx guidance currently available and which may be considered as potential alternative treatment options.

CLASS	MEDICATION	PGx GUIDANCE			ALTERNATIVES WITH NO PGx GUIDANCE
		USE STANDARD PRECAUTIONS	USE WITH CAUTION	CONSIDER ALTERNATIVE	USE STANDARD PRECAUTIONS
Alpha-Blockers for Benign Prostatic Hyperplasia	Alfuzosin^				✓
	Doxazosin^				✓
	Silodosin^				✓
	Tamsulosin	✓			
Angiotensin II Receptor Antagonists	Candesartan^				✓
	Eprosartan^				✓
	Irbesartan	✓			
	Losartan	✓			
	Olmesartan^				✓
	Telmisartan^				✓
	Valsartan^				✓
Antiaddictives	Naltrexone	✓			
Anti-ADHD Agents	Atomoxetine		!		
	Clonidine		!		
	Dextroamphetamine	✓			
	Guanfacine^				✓
	Lisdexamfetamine	✓			
Antiarrhythmics	Flecainide			✗	
Anticoagulants	Apixaban^				✓
	Dabigatran Etexilate^				✓
	Fondaparinux^				✓
	Rivaroxaban^				✓
	Warfarin	✓			

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		USE STANDARD PRECAUTIONS	USE WITH CAUTION	CONSIDER ALTERNATIVE	USE STANDARD PRECAUTIONS
Anticonvulsants	Brivaracetam	✓			
	Cannabidiol^				✓
	Carbamazepine^				✓
	Ethosuximide^				✓
	Gabapentin^				✓
	Lacosamide	✓			
	***Lamotrigine*^**				✓
	Levetiracetam^				✓
	Oxcarbazepine^				✓
	Perampanel^				✓
	Phenobarbital	✓			
	Phenytoin	✓			
	Pregabalin^				✓
	Primidone	✓			
	Rufinamide^				✓
	Tiagabine^				✓
	Topiramate^				✓
	Valproic Acid^				✓
	Vigabatrin^				✓
	Zonisamide	✓			
Antidementia Agents	Donepezil		!		
	Galantamine	✓			

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		USE STANDARD PRECAUTIONS	USE WITH CAUTION	CONSIDER ALTERNATIVE	USE STANDARD PRECAUTIONS
Antidepressants	Amitriptyline			✗	
	Citalopram			✗	
	Clomipramine			✗	
	Desvenlafaxine	✓			
	Doxepin			✗	
	Duloxetine	✓			
	Escitalopram			✗	
	Fluoxetine	✓			
	Fluvoxamine		!		
	Imipramine			✗	
	Mirtazapine	✓			
	Nortriptyline			✗	
	Paroxetine			✗	
	Sertraline		!		
	Trazodone^				✓
	Venlafaxine			✗	
	Vortioxetine	✓			
Antiemetics	Dolasetron		!		
	Fosaprepitant^				✓
	Fosnetupitant-Palonosetron		!		
	Granisetron		!		
	Metoclopramide	✓			
	Ondansetron			✗	
	Palonosetron		!		
Antifungals	Amphotericin B^				✓
	Anidulafungin^				✓
	Caspofungin^				✓
	Fluconazole^				✓
	Itraconazole^				✓
	Micafungin^				✓
	Posaconazole^				✓
	Voriconazole			✗	

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Anti-Hyperuricemics and Anti-Gout Agents	Colchicine^				✓
	Febuxostat^				✓
	Lesinurad	✓			
Antimalarials	Proguanil	✓			
Antiplatelets	Clopidogrel		!		
	Prasugrel^				✓
	Ticagrelor^				✓
Antipsychotics	Aripiprazole	✓			
	Asenapine^				✓
	Brexpiprazole	✓			
	Chlorpromazine		!		
	Clozapine		!		
	Haloperidol			✗	
	Lurasidone^				✓
	Olanzapine		!		
	Paliperidone	✓			
	Periciazine^				✓
	Quetiapine^				✓
	Risperidone			✗	
	Trifluoperazine^				✓
	Ziprasidone^				✓
	Zuclopenthixol			✗	
Antispasmodics for Overactive Bladder	Darifenacin	✓			
	Mirabegron	✓			
	Oxybutynin^				✓
	Solifenacin^				✓
	Tolterodine	✓			
Benzodiazepines	Alprazolam^				✓
	Clobazam	✓			
	Clonazepam^				✓
	Diazepam		!		

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Beta Blockers	Atenolol^				✓
	Bisoprolol^				✓
	Carvedilol	✓			
	Labetalol^				✓
	Metoprolol			✗	
	Nebivolol	✓			
	Propranolol	✓			
	Timolol	✓			
Endocrine-Metabolic Agents	Eliglustat			✗	
	Imiglucerase^				✓
	Miglustat^				✓
	Taliglucerase alfa^				✓
	Velaglucerase alfa^				✓
Immunomodulators	Apremilast^				✓
	Leflunomide	✓			
	Tofacitinib	✓			
Immunosuppressants	Tacrolimus	✓			
NSAIDs	Celecoxib	✓			
	Diclofenac	✓			
	Flurbiprofen	✓			
	Ibuprofen	✓			
	Indomethacin	✓			
	Ketoprofen^				✓
	Ketorolac^				✓
	Meloxicam	✓			
	Naproxen^				✓
	Piroxicam	✓			
	Sulindac^				✓

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		USE STANDARD PRECAUTIONS	USE WITH CAUTION	CONSIDER ALTERNATIVE	USE STANDARD PRECAUTIONS
Opioids	Alfentanil^				✓
	Buprenorphine^				✓
	Codeine			✗	
	Dihydrocodeine		!		
	Fentanyl		!		
	Hydromorphone^				✓
	Morphine		!		
	Oxycodone		!		
	Tapentadol^				✓
	Tramadol			✗	
Other Neurological Agents	Tetrabenazine		!		
Proton Pump Inhibitors	Esomeprazole		!		
	Lansoprazole		!		
	Omeprazole		!		
	Pantoprazole		!		
	Rabeprazole	✓			
Statins	Atorvastatin		!		
	Fluvastatin	✓			
	Pitavastatin		!		
	Pravastatin		!		
	Rosuvastatin		!		
	Simvastatin			✗	
Sulfonylureas	Glimepiride	✓			
	Glipizide	✓			

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3 Dosing Guidance

Amitriptyline

Decreased Amitriptyline Exposure (CYP2C19: Rapid Metabolizer) — INFORMATIVE

The patient's high CYP2C19 activity is likely to result in a significantly increased metabolism of amitriptyline to nortriptyline and a subsequent decrease in amitriptyline exposure leading to therapy failure or increased side effects.

Psychiatric Conditions: Consider an alternative medication. If amitriptyline is warranted, consider therapeutic drug monitoring to guide dose adjustments.

Neuropathic Pain: Consider an alternative medication. If amitriptyline is warranted titrate dose according to the patient's clinical response and tolerability.

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

Decreased Clomipramine Exposure (CYP2C19: Rapid Metabolizer) — INFORMATIVE

The patient's high CYP2C19 activity is likely to result in a significantly increased metabolism of clomipramine to desmethyl clomipramine and a subsequent decrease in clomipramine exposure leading to therapy failure or increased side effects.

Psychiatric Conditions: Consider an alternative medication. If clomipramine is warranted, consider therapeutic drug monitoring to guide dose adjustments.

Codeine

Increased Response to Codeine (CYP2D6: Ultra-Rapid Metabolizer) — ACTIONABLE

Codeine is converted into its active metabolite morphine by CYP2D6. Since this patient is a ultra-rapid metabolizer, greatly increased morphine levels are expected, and the patient is at high risk of toxicity when taking codeine. The ultra-rapid conversion of codeine to morphine in breast feeding mothers can result in high and unsafe levels of morphine in the breast milk potentially causing life threatening respiratory depression in the breastfed infant. Avoid prescribing codeine, and consider an alternative opioid 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.

Doxepin

Decreased Doxepin Exposure (CYP2C19: Rapid Metabolizer) — INFORMATIVE

The patient's high CYP2C19 activity is likely to result in a significantly increased metabolism of doxepin to desmethyl doxepin and a subsequent decrease in doxepin exposure leading to therapy failure or increased side effects.

Psychiatric Conditions: Consider an alternative medication. If doxepin is warranted, consider therapeutic drug monitoring to guide dose adjustments.

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

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Eliglustat

Possible Non-Response to Eliglustat (CYP2D6: Ultra-Rapid Metabolizer) — ACTIONABLE

CYP2D6 ultra-rapid metabolizers may not reach adequate concentrations of eliglustat to achieve a therapeutic effect. Eliglustat should not be prescribed in patients who are CYP2D6 ultra-rapid metabolizers. An alternative medication may be considered.

Escitalopram

Insufficient Response 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.

Flecainide

Altered Response to Flecainide (CYP2D6: Ultra-Rapid Metabolizer) — ACTIONABLE

Titrate carefully and consider adjusting the dose in response to plasma concentration and ECG monitoring, OR consider an alternative drug. Examples of alternatives drugs not affected by CYP2D6 include: sotalol, disopyramide, quinidine, and amiodarone.

Haloperidol

Non-Response to Haloperidol (CYP2D6: Ultra-Rapid Metabolizer) — ACTIONABLE

Consider an alternative drug, or prescribe haloperidol at the standard dose and adjust dosage to achieve a favorable clinical response. Be alert to decreased haloperidol plasma concentrations.

Imipramine

Decreased Imipramine Exposure (CYP2C19: Rapid Metabolizer) — INFORMATIVE

The patient's high CYP2C19 activity is likely to result in a significantly increased metabolism of imipramine to desipramine and a subsequent decrease in imipramine exposure leading to therapy failure or increased side effects.

Psychiatric Conditions: Consider an alternative medication. If imipramine is warranted, consider therapeutic drug monitoring to guide dose adjustments.

Metoprolol

Possible Non-Responder to Metoprolol (CYP2D6: Ultra-Rapid Metabolizer) — ACTIONABLE

The patient may experience a decrease in the pharmacological effect when taking metoprolol at standard dosage. Heart Failure: Consider alternative beta-blockers such as bisoprolol or carvedilol, or prescribe metoprolol at a higher dose. Other indications: Consider alternative beta-blockers such as bisoprolol or atenolol, or prescribe metoprolol at a higher dose. If metoprolol is prescribed, titrate the dose to a maximum of 250% of the normal dose in response to efficacy and adverse events.

Nortriptyline

Decreased Nortriptyline Exposure (CYP2D6: Ultra-Rapid Metabolizer) — ACTIONABLE

The patient is predicted to be a CYP2D6 ultra-rapid metabolizer which is likely to result in a significantly increased metabolism of nortriptyline to less active compounds and a subsequent decrease in nortriptyline exposure leading to therapy failure.

Psychiatric Conditions: Consider an alternative medication. If nortriptyline is warranted, consider increasing the recommended dose and use therapeutic drug monitoring to guide dose adjustments.

EXAMPLE

Ondansetron

Non-Response to Ondansetron (CYP2D6: Ultra-Rapid Metabolizer) ACTIONABLE

A substantially decreased antiemetic effect has been reported in CYP2D6 ultra-rapid metabolizers when taking standard doses of this medication. Consider prescribing an alternative drug not metabolized by CYP2D6 such as granisetron.

Paroxetine

Reduced Response to Paroxetine (CYP2D6: Ultra-Rapid Metabolizer) ACTIONABLE

There is a risk for decreased efficacy at standard dosage. If a standard dose is prescribed to a CYP2D6 ultra-rapid metabolizer, suboptimal plasma concentrations of the drug are likely. Consider an alternative medication.

Risperidone

Non-Response to Risperidone (CYP2D6: Ultra-Rapid Metabolizer) ACTIONABLE

Consider an alternative drug, OR prescribe risperidone , be extra alert to insufficient response, and adjust dosage in response to clinical response and adverse events.

Simvastatin

Intermediate Myopathy Risk (SLCO1B1: Decreased Function) ACTIONABLE

Simvastatin plasma concentrations are expected to be elevated. Consider avoiding simvastatin, and prescribe an alternative statin or another hypolipidemic drug, or consider prescribing simvastatin at a lower starting dose (20 mg/day). Routine creatine kinase (CK) monitoring is also advised. The FDA recommends against the 80 mg daily dose. Although the association between the SLCO1B1 521T>C variant and myopathy risk is not clearly established for other statins such as atorvastatin, pitavastatin, rosuvastatin, and pravastatin, caution is advised if high doses of these statins are used in this patient. Fluvastatin plasma levels are not affected by the SLCO1B1 521T>C variant.

Tramadol

Increased Response to Tramadol (CYP2D6: Ultra-Rapid Metabolizer) ACTIONABLE

The patient is at high risk of toxicity when taking tramadol at standard dosing. Consider reducing tramadol dose by 30%. Careful monitoring for side effects (nausea, vomiting, constipation, respiratory depression, confusion, urinary retention) and weekly titration are recommended. In case of toxicity, 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.

The accelerated conversion of tramadol to its active metabolite can result in high and unsafe levels of this metabolite in breast milk potentially causing life threatening respiratory depression in the breastfed infant. Use of tramadol should be avoided in breastfeeding mothers.

Venlafaxine

Non-Response to Venlafaxine (CYP2D6: Ultra-Rapid Metabolizer) ACTIONABLE

The patient is unlikely to achieve adequate serum levels of venlafaxine and O-desmethylvenlafaxine when taking standard doses of venlafaxine. Consider an alternative drug, or increase the venlafaxine dose to a maximum of 150% of the normal dose and monitor venlafaxine and O-desmethylvenlafaxine plasma concentrations.

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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.

Zuclopenthixol

Non-Response to Zuclopenthixol (CYP2D6: Ultra-Rapid Metabolizer) — INFORMATIVE

Based on the genotype result, this this patient may be at risk of therapy failure when taking zuclopenthixol at standard dosage. Consider using this drug with close monitoring of plasma concentrations and titrate dose in response to the clinical effect, or consider an alternative medication. Unless contraindicated, alternative medications include flupenthixol, clozapine, olanzapine or quetiapine.

Atomoxetine

Possible Atomoxetine Underexposure Leading to Decreased Response (CYP2D6: Ultra-Rapid Metabolizer) — ACTIONABLE

The genotype result indicates that the patient is likely to have an insufficient response due to inadequate drug exposure following standard dosing. Consider the following dosing strategy:

- Initiate treatment at 40 mg/day, increase to 80 mg/day after 3 days and maintain dose.
- 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 2 weeks, optimal clinical response is not observed and adverse events are not present, consider therapeutic drug monitoring 1-2 hours post dose. If the plasma concentration is less than 200 ng/ml consider a dose increase to a target of 400 ng/ml. Doses greater than 100 mg/day may be needed to achieve a targeted therapeutic concentration. (Therapeutic range: 200-1000 ng/ml).

Atorvastatin

Increased Myopathy Risk (SLCO1B1: Decreased Function) — INFORMATIVE

The reduced SLCO1B1 function may result in elevated atorvastatin plasma levels. Because the risk of myopathy increases in patients with high statin plasma levels, the use of high atorvastatin doses in this patient should be avoided. If atorvastatin is used in this patient, a closer monitoring of serum creatine kinase and liver function is recommended. Other myopathy predisposing factors include advanced age (≥65), uncontrolled hypothyroidism, renal impairment, comedications, and female gender.

Chlorpromazine

Possible Non-Response to Chlorpromazine (CYP2D6: Ultra-Rapid Metabolizer) — INFORMATIVE

Chlorpromazine is metabolized by CYP2D6, CYP3A4 and flavin-containing monooxygenases. Subjects with increased CYP2D6 function will metabolize chlorpromazine more rapidly which can result in sub-therapeutic drug concentrations. Consider a standard dose and adjust dosage according to the patient's tolerability and response. Higher doses may be necessary to achieve efficacy.

Clonidine

Possible Altered Response to Clonidine (CYP2D6: Ultra-Rapid Metabolizer) — INFORMATIVE

Treatment with clonidine can cause dose related decreases in blood pressure and heart rate Measure heart rate and blood pressure prior to initiation of therapy, following dose increases, and periodically while on therapy. Titrate Clonidine slowly in patients with a history of hypotension, and those with underlying conditions that may be worsened by hypotension and bradycardia.

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.

EXAMPLE

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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.

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.

Dihydrocodeine

Possible Altered Response to Dihydrocodeine (CYP2D6: Ultra-Rapid Metabolizer) — INFORMATIVE

Increased conversion of dihydrocodeine to the more active metabolite dihydromorphine is expected in CYP2D6 ultra-rapid metabolizers. This may result in an exaggerated response. Adequate pain relief can be achieved by decreasing the dose in response to pain symptoms. Other opioids not metabolized by CYP2D6 (i.e., morphine, oxymorphone, buprenorphine, fentanyl, methadone, and hydromorphone) may also be considered if signs of overdose (excessive sleepiness, confusion, or shallow breathing) are reported.

Dolasetron

Possible Altered Response to Dolasetron (CYP2D6: Ultra-Rapid Metabolizer) — INFORMATIVE

The reduction of dolasetron to its active metabolite hydrodolasetron is mediated by a carbonyl reductase. Hydrodolasetron is further eliminated by multiple routes, including renal excretion and by glucuronidation or hydroxylation by CYP2D6. Compared to CYP2D6 normal metabolizers, CYP2D6 ultra-rapid metabolizers may have lower hydroxydolasetron plasma concentrations at standard dosing. However, the clinical significance of this change remains unclear. Dolasetron can be prescribed at standard label-recommended dosage and administration. Monitor the patient for possible decreased efficacy.

Donepezil

Possible Altered Response to Donepezil (CYP2D6: Ultra-Rapid Metabolizer) — INFORMATIVE

When compared to a normal metabolizer, a ultra-rapid metabolizers has a 24% increase in donepezil clearance. The clinical significance of this increase is not well documented. Consider using a standard dosing regimen and adjust dosage in response to clinical response and tolerability.

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%.

Fentanyl

Altered Response to Fentanyl (OPRM1: Altered OPRM1 Function) — INFORMATIVE

The patient carries one copy of the OPRM1 118A>G variant. Acute postoperative and cancer pain: the patient's genotype has been shown to be associated with reduced analgesia at standard fentanyl doses. Therefore, the patient may require higher doses of this drug. Because fentanyl has a narrow therapeutic window, it is advised to carefully titrate this drug to a tolerable dose that provides adequate analgesia with minimal side effects.

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Fluvoxamine

Possible Reduced Response to Fluvoxamine (CYP2D6: Ultra-Rapid Metabolizer) — INFORMATIVE

There is a risk for decreased efficacy at standard dosage. If a standard dose is prescribed to a CYP2D6 ultra-rapid metabolizer, suboptimal plasma concentrations of the drug are likely. There is insufficient data to calculate dose adjustments and careful titration is recommended until a favorable response is achieved. An alternative medication not metabolized by CYP2D6 can also be considered.

Fosnetupitant-Palonosetron

Possible Altered Response to Fosnetupitant-Palonosetron (CYP2D6: Ultra-Rapid Metabolizer) — INFORMATIVE

Fosnetupitant: Fosnetupitant is converted to netupitant via metabolic hydrolysis. Netupitant is extensively metabolized to three major metabolites (desmethyl, N-oxide and a hydroxy-methyl derivatives). Metabolism is mediated primarily by CYP3A4 and to a lesser extent by CYP2C9 and CYP2D6. No genetically guided drug selection or dosing recommendations are available for this drug. Fosnetupitant can be prescribed at standard label-recommended dosage and administration.
Palonosetron: Palonosetron is eliminated by multiple routes including metabolism. While CYP2D6 and to a lesser extent, CYP3A4 and CYP1A2 are involved in its metabolism to two inactive metabolites. Compared to CYP2D6 normal metabolizers, CYP2D6 ultra-rapid metabolizers may have lower palonosetron plasma concentrations at standard dosing. However, the clinical significance of this change remains unclear. Palonosetron can be prescribed at standard label-recommended dosage and administration. Monitor the patient for possible decreased efficacy.

Granisetron

Unfavorable Response to Standard Granisetron Dosing (ABCB1: Variant Allele Not 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.

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%.

Morphine

Altered Response to Morphine (OPRM1: Altered OPRM1 Function) — INFORMATIVE

The patient carries one copy of the OPRM1 118A>G variant. Acute postoperative and cancer pain: the patient's genotype has been shown to be associated with possible reduced analgesia at standard morphine doses and decreased risk for nausea and vomiting during the first 24-hour postoperative period. Therefore, the patient may require higher doses of this drug. The dosing regimen needs to be individualized for each patient, taking into account the patient's prior analgesic treatment experience.

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%.

Oxycodone

Possible Altered Response to Oxycodone (CYP2D6: Ultra-Rapid Metabolizer) — ACTIONABLE

Increased conversion of oxycodone to the more active metabolite oxymorphone is expected in CYP2D6 ultra-rapid metabolizers. Usually, adequate pain relief without an increase in adverse events can be achieved by using standard or lower oxycodone doses. Other opioids not metabolized by CYP2D6 (e.g., morphine, oxymorphone, buprenorphine, fentanyl, methadone, and hydromorphone) may also be considered if excessive side effects are reported.

Palonosetron

Possible Altered Response to Palonosetron (CYP2D6: Ultra-Rapid Metabolizer) — INFORMATIVE

Palonosetron is eliminated by multiple routes including metabolism. While CYP2D6 and to a lesser extent, CYP3A4 and CYP1A2 are involved in its metabolism to two inactive metabolites. Compared to CYP2D6 normal metabolizers, CYP2D6 ultra-rapid metabolizers may have lower palonosetron plasma concentrations at standard dosing. However, the clinical significance of this change remains unclear. Palonosetron can be prescribed at standard label-recommended dosage and administration. Monitor the patient for possible decreased efficacy.

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%.

Pitavastatin

Increased Myopathy Risk (SLCO1B1: Decreased Function) — INFORMATIVE

The reduced SLCO1B1 function may result in elevated pitavastatin plasma levels. Because the risk of myopathy increases in patients with high statin plasma levels, the use of high pitavastatin doses in this patient should be avoided. If pitavastatin is used in this patient, a closer monitoring of serum creatine kinase and liver function is recommended. Other myopathy predisposing factors include advanced age (≥65), uncontrolled hypothyroidism, renal impairment, comedications, and female gender.

Pravastatin

Increased Myopathy Risk (SLCO1B1: Decreased Function) — INFORMATIVE

The reduced SLCO1B1 function may result in elevated pravastatin plasma levels. Because the risk of myopathy increases in patients with high statin plasma levels, the use of high pravastatin doses in this patient should be avoided. If pravastatin is used in this patient, a closer monitoring of serum creatine kinase and liver function is recommended. Other myopathy predisposing factors include advanced age (≥65), uncontrolled hypothyroidism, renal impairment, comedications, and female gender.

Rosuvastatin

Increased Myopathy Risk (SLCO1B1 521T>C T/C) — INFORMATIVE

The reduced SLCO1B1 function may result in elevated rosuvastatin plasma levels. Because the risk of myopathy increases in patients with high statin plasma levels, the use of high rosuvastatin doses in this patient should be avoided. If rosuvastatin is used in this patient, a closer monitoring of serum creatine kinase and liver function is recommended. Other myopathy predisposing factors include advanced age (≥65), uncontrolled hypothyroidism, renal impairment, comedications, and female gender.

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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.

Tetrabenazine

Unknown Sensitivity to Tetrabenazine (CYP2D6: Ultra-Rapid Metabolizer) — ACTIONABLE

For treating chorea associated with Huntington's disease: There is insufficient data to calculate dose adjustment, and if tetrabenazine is prescribed, 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 ultra-rapid metabolizers is not defined. The maximum daily dose in normal metabolizers 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.

EXAMPLE

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Sample Patient
LAB ID 987654321 DOB 23/07/1979 (39Y Female)
Referring Doctor Dr Kate Goodhealth
Reported 26 Sep 2019 06:40 am

4 Test details

GENE	GENOTYPE	PHENOTYPE	ALLELES TESTED
CYP2D6	*1/*1 XN	Ultra-Rapid 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/A	Intermediate Warfarin Sensitivity	-1639G>A
ABCB1	3435C>T C/C	Variant Allele Not Present	3435C>T
OPRM1	A118G A/G	Altered OPRM1 Function	A118G
SLCO1B1	521T>C T/C	Decreased Function	521T>C

EXAMPLE

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 ddPCR specific for exon 9 (BIO-RAD). 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. The pharmacogenomic guidance in this Sonic PGx Panel report has been validated in adult patients. Caution should be applied when interpreting this report for patients under 18 years of age.

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.