

Information for Doctors

Understanding the Sonic PGx report

The Sonic PGx Panel checks for the presence of more than 60 significant variants in 10 genes involved in the metabolism of, or response to, more than 80 common medications.

The report can be used immediately to guide the prescribing of medications a patient is currently taking or to inform the choice of new medications, providing both short- and long-term advice. The report is also relevant for other gene-medication combinations that may influence a patient's health in the future.

For improved understanding and interpretation, the report follows a set structure, as outlined below.

1. Answering the immediate question

When the request form specifies the medications the patient is currently taking, or medications being considered by the requesting doctor, the first section of the report provides explicit prescribing advice for these medications.







For example, in this patient, escitalopram and venlafaxine are unlikely to provide therapeutic benefit and alternative medications are recommended ☒. The term **ACTIONABLE** indicates that there is strong clinical evidence for this advice, based on clinical implementation guidelines.* Alternative medications are suggested in the next section of the report.

On the other hand, there is no contraindication to prescribing lamotrigine, according to these guidelines: ☑. However, as explained in the text, this advice is **INFORMATIVE** rather than **ACTIONABLE**, meaning that the clinical evidence base for the advice is less strong.

Olazapine is in a third category of prescribing advice, which is to take an intermediate approach !. The advice may include recommending a change in dose or increased monitoring of response and for side effects.

In our experience, one in five patients with medications specified on the request form has a ☒ **DO NOT USE** caution in this section of the report. And one in three patients has a ! **USE WITH CAUTION** response in this section.

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 UGT2B7. 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. Co-administration 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.			
	 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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2. Advice regarding other medications

The second section of the report lists more than 80 common medications, and provides a simple summary of the prescribing advice based on the patient's genetic test. The medications are listed alphabetically by indication and then by generic medication name.

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*				✓
	Tamulosin	✓			
	Candesartan*				✓
Angiotensin II Receptor Antagonists	Eprosartan*				✓
	Irbesartan	✓			
	Losartan	✓			
	Olmesartan*				✓
	Telmisartan*				✓
	Valsartan*				✓
Antiaddictives	Naltrexone	✓			
	Atomoxetine		!		
Anti-ADHD Agents	Clonidine				
	Dextroamphetamine	✓			
	Guafacine*				✓
	Lisdexamfetamine	✓			

For each medication, the summary indicates whether the prescribing advice is:

- ✗ Consider an alternative medication
- ! Use with caution
- ✓ Usual prescribing practice

There are also many common medications for which pharmacogenomics has been shown to not inform prescribing decisions; these medications are indicated in the far right column as requiring the usual cautions ✓.

This list of medications extends over a number of pages, and is primarily a resource for future prescribing. This list is helpful when considering alternative medications for a patient because it provides pharmacogenomic advice for multiple medications that have the same indication.

DO NOT USE caution in this section of the report. And three in four patients will have at least one ! USE WITH CAUTION response in this section of the report.

3. Detailed advice about other medications

The third section of the report provides detailed advice about any medications that have a ✗ DO NOT USE or ! USE WITH CAUTION response in Part 2. It is a good resource for detailed prescribing advice in the future.

As before, the strength of the evidence base is indicated by the advice being **ACTIONABLE** (strong evidence for this advice) or **INFORMATIVE** (less strong evidence base for this advice).

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.	

4. Genetic details

The final section of the report summarises the genetic results, that is, the genes tested, the variants identified in each gene (genotype), the predicted effect on enzyme or receptor activity (phenotype), and the variants in each gene included in the analysis.

The Sonic PGx Panel report informs, rather than dictates, prescribing decisions.
Be sure to consider all relevant factors required to make appropriate prescribing decisions.

For further details, please refer to the Sonic Genetics website, www.sonicgenetics.com.au, speak with your local Client Liaison or contact Sonic Genetics on 1800 010 447 or email info@sonicgenetics.com.au.

*The recommendations are from evidence-based guidelines issued by international pharmacogenetic consortia, professional societies and regulatory bodies (Clinical Pharmacogenetics Implementation Consortium, Dutch Pharmacogenetics Working Group, US Food & Drug Administration, European Medicines Agency, Canadian Pharmacogenomics Network for Drug Safety, American College of Medical Genetics & Genomics).

*Correct at time of printing.