

# PHARMACOGENOMIC TESTING

**TAILORING  
MEDICATION FOR  
EVERY PATIENT**

**Achieve treatment goals sooner with  
pharmacogenomic - guided prescribing**

# TAILORING MEDICATION FOR EVERY INDIVIDUAL

*Achieve treatment goals sooner with more informed prescribing.*

## What is pharmacogenomics (PGx)?

PGx is the study of genetic variations that influence medication response. PGx is now enabling doctors to test for specific genetic changes to predict whether a patient may have a normal response, a poor response, or a higher risk of side effects before prescribing a specific medication.

## NOT ALL PATIENTS RESPOND TO THE SAME MEDICATION EQUALLY.

Common genetic variations in the genes encoding drug metabolising enzymes (e.g. Cytochrome P450 enzymes) can result in changes to the activity of the enzyme. Reduced metabolism in intermediate and poor metabolisers results in accumulation of the substrate drug, leading to an increased risk of side effects and toxicity from standard doses. Overly efficient elimination of the substrate drug in rapid and ultrarapid metabolisers leads to less medication being available for clinical effect, and potentially therapeutic failure.

These extremes of metabolism are commonly found in the Australian population as reported in a study of 5408 Australian patients' genotyped for CYP2D6, CYP2C19 and CYP2C9 enzymes, with frequencies displayed in the table below.<sup>3</sup>

The diagram also shows that over 60% of the population are not normal metabolisers for CYP2C19, and consequently may require adjustments when being prescribed certain medications to achieve treatment goals. Traditional prescribing by trial and error may result in toxic, adverse, or sub-therapeutic effects for a significant group of patients. Pharmacogenetic results can therefore inform doctors to adjust medications and dosage more appropriately.

ENZYME	POOR METABOLISER	INTERMEDIATE METABOLISER	HIGH INTERMEDIATE METABOLISER	LOW NORMAL METABOLISER	NORMAL METABOLISER	RAPID METABOLISER	ULTRARAPID METABOLISER
CYP2D6	5.7%	11.7%	–	26.2%	53.2%	–	2.8%
CYP2C19	3.1%	20.9%	6.3%	–	39.7%	25.8%	4.2%
CYP2C9	4.2%	10.6%	20.4%	–	64.8%	–	–

## INCREASING ENZYME ACTIVITY

**Table 1:** Population frequency of different metaboliser categories for key genes involved in drug metabolism.

## WHAT IS THE SUPPORTING EVIDENCE FOR THE CLINICAL APPLICATION OF PGx?

The PGx medication reports are based on the results of many clinical studies that measure how genetic variations affect a drug's efficacy and/or risk of adverse effects. Recently, the results of these studies have been confirmed by an increasing number of randomised controlled trials (RCTs). These studies have been recently summarised into published guidelines by the Clinical Pharmacogenetics Implementation Consortium (CPIC) and the Royal Dutch Pharmacists Association – Pharmacogenetics Working Group.

Guidelines are routinely updated, peer reviewed, and published in relevant journals. See below examples that contain evidence for gene-drug associations, for which dosage adjustments have been recommended:

- **CPIC guidelines for Tricyclic Antidepressants, Selective Serotonin Reuptake Inhibitors (SSRIs) and Codeine<sup>1</sup>**
- **Dutch Pharmacogenetics Working Group guidelines which include a number of antidepressant and antipsychotic medications<sup>7</sup>**

The US Food and Drug Administration (FDA) has also published a list of over 150 drug labels with warnings based on pharmacogenomic biomarkers<sup>2</sup>.

## WHAT ARE THE CLINICAL BENEFITS?

- Reduce the risk of adverse drug reactions;
- Reduce wasted cost and time on 'trial & error' medicines;
- Lifetime relevance—results can be referred to for subsequent treatment; and
- Help to reach treatment goals sooner

## WHICH PATIENTS BENEFIT FROM PGx TESTING?

All patients may benefit from PGx testing, however some patients are more likely to see an immediate benefit from PGx testing, including those:

- Experiencing side effects to specific medications;
- Not responding to specific medications;
- Requiring doses of specific medications outside the recommended range; and
- Taking multiple medications.

# DID YOU KNOW?

1 IN 5

Australians suffer from persistent pain, making their risk of depression 4x higher than those without pain.<sup>6</sup>

50% OF PATIENTS

respond to the initial treatment with antidepressants.<sup>4</sup>

1 IN 10 PEOPLE

may process certain medications too slowly, increasing their risk of side effects.<sup>5</sup>

1 IN 3 PEOPLE

may process certain medications too quickly, increasing their risk of treatment failure.<sup>5</sup>

## PGx MEDICATION TEST

Genomic Diagnostics is a leading provider of genetic pathology testing in Australia. Access to our services is enabled through our state-based pathology network including TML Pathology, Lavery Pathology, Queensland Medical Laboratories, Abbott Pathology, Dorevitch Pathology and Western Diagnostic Pathology.

In order to provide advanced and value-added pharmacogenetic capabilities to our practitioners, we have partnered with myDNA Life Australia. Their experience combined with access to pharmacogenomic clinical support and online education resources delivers more for clinicians in this emerging testing environment.

### PGx MENTAL HEALTH (PGx MH)

The PGx MH test analyses a specific group of genes that are known to be involved in drug metabolism for a broad range of psychotropic medications used to treat a variety of psychiatric disorders. The report provides detailed interpretation and prescribing recommendations for many antidepressants, antipsychotics and some ADHD medications and anxiolytics, all of which are listed in Table 2.

### PGx PAIN

The PGx Pain test analyses a specific group of genes that are known to affect the drug response to several analgesics used to treat different types of pain. The report provides detailed interpretation and prescribing recommendations for several opioid analgesics, non-steroidal anti-inflammatory drugs (NSAIDs) and some medications used for neuropathic pain, all of which are listed in Table 3.

### PGx MULTI

The PGx Multi test analyses variations in genes that have been shown to influence drug response and metabolism for over 80 medications used in clinical practice and includes all genes present in PGx MH and PGx PAIN. Given many patients are on multiple medications, you may find the PGx Multi report most useful as it covers a broad range of medication classes. The report provides medication-specific prescribing considerations which may help to improve the safety and efficacy of medications and reduce the risk of unwanted side effects.

### KEY EXAMPLES OF MEDICATIONS INFLUENCED BY GENES IN PGx, MH OR PGx PAIN

MENTAL HEALTH MEDICATION		
Antidepressants		
Agomelatine	Escitalopram	Nortriptyline
Amitriptyline	Fluoxetine	Paroxetine
Citalopram	Fluvoxamine	Sertraline
Clomipramine	Imipramine	Venlafaxine
Dothiepin	Mianserin	Vortioxetine
Doxepin	Mirtazapine	
Duloxetine	Moclobemide	
Antipsychotics		Other
Aripiprazole	Olanzapine	Atomoxetine
Brexipiprazole	Quetiapine	Clobazam
Chlorpromazine	Risperidone	Diazepam
Clozapine	Zuclopenthixol	Melatonin
Haloperidol		

Table 2: Key examples of psychotropic medications influenced by genetics.

PAIN MEDICATION		
NSAIDs	Opioid Analgesics	Other
Celecoxib	Codeine	Amitriptyline
Ibuprofen	Morphine	Duloxetine
Meloxicam	Oxycodone	Nortriptyline
Piroxicam	Tramadol	

Table 3: Key examples of analgesic medications influenced by genetics.

**For information on medications relevant to the PGx Multi test, please review the Medication Report Quick Reference List**



# How to order?

- 1 Discuss **PGx Medication test** with your patient. Order the test using the standard pathology request form. Select:

PGx Pain (\$147\*)

PGx MH (\$147\*)

PGx Multi (\$197\*)

**Remember to list patient's medications.**

- 2 Patient directed to pay for the test via: [www.gdpay.com.au](http://www.gdpay.com.au) prior to visiting collection centre and record the receipt number on request form. This test has NO Medicare rebate.
- 3 Patient visits **TML Pathology Collection Centre** with request for blood collection.
- 4 **Results will be delivered to you via your preferred method.** This test has an approximate 2 week turn around time.
- 5 **View full PDF.** This will provide you with further recommendations and insights by using the link within the patient's report. You will need to be registered for this portal by your TML Pathology representative or by Genomic Diagnostics. Please call 1800 822 999 or email [info@genomicdiagnostics.com.au](mailto:info@genomicdiagnostics.com.au)
- 6 **Print report for patient.** You can provide your patient with secure online access to a pdf version of their report via the instructions and unique patient access ID at the end of the test report.

## TEST LIMITATIONS

There are some important test limitations to be aware of:

- The test cannot determine how individuals respond to all medications in clinical use (see medication quick reference list).
- Response to medications is complex and may also be influenced by factors which are not tested for (e.g. compliance, concurrent illness, drug-drug interactions.). The test only determines response to indicated medications (see quick reference list).
- Allergic reactions cannot be detected by this genetic test.
- The test does not detect all known variants in the genes tested. Only common variants present in Caucasian, African and Asian backgrounds are covered.
- If an individual carries a rare variant not covered by the test, the phenotype may be inaccurately reported. Testing for the common variants is the practice of most screening molecular genetic testing laboratories around the world.

For more information please call

**1800 822 999**

or email [info@genomicdiagnostics.com.au](mailto:info@genomicdiagnostics.com.au)

or visit [www.genomicdiagnostics.com.au](http://www.genomicdiagnostics.com.au)

### References:

1. The CPIC guidelines are publicly available at: <https://cpicpgx.org/guidelines/>
  2. The FDA drug labels are available publicly at: <https://www.fda.gov/drugs/scienceresearch/ucm572698.htm>
  3. Mostafa S, Kirkpatrick CMJ, Byron K, Sheffield L. An analysis of allele, genotype and phenotype frequencies, actionable pharmacogenomic (PGx) variants and phenoconversion in 5408 Australian patients genotyped for CYP2D6, CYP2C19, CYP2C9 and VKORC1 genes. J Neural Transm [journal on the internet]. 2018 Sep 6 [cited 2018 Dec 6]. Available from: <https://link.springer.com/article/10.1007%2Fs00702-018-1922-0> [Epub ahead of print]
  4. Rush AJ, Trivedi MH, Wisniewski SR, Nierenberg AA, Stewart JW, Warden D, et al. Acute and longer-term outcomes in depressed outpatients requiring one or several treatment steps: a STAR\*D report. Am J Psychiatry. 2006;163(11):1905-17.
  5. Hicks JK, Sangkuhl K, Swen JJ, Ellingrod VL, Muller DJ, Shimoda K, et al. Clinical pharmacogenetics implementation consortium guideline (CPIC) for CYP2D6 and CYP2C19 genotypes and dosing of tricyclic antidepressants: 2016 update. Clin Pharmacol Ther. 2017;102(1):37-44.
  6. Painaustralia (accessed 2019) <https://www.painaustralia.org.au/static/uploads/files/mr-mental-health-week-102017-final-wfdqwahtcgj.pdf>
  7. Swen J, Nijenhuis M, de Boer A, Grandia L, Maitland-van der Zee A, Mulder H et al. Pharmacogenetics: From Bench to Byte— An Update of Guidelines. Clin Pharmacol Ther. 2011;89(5):662-673.
- \* Prices valid at February, 2019. Prices are subject to change and will be reviewed at regular intervals. For latest pricing, please see our website: [www.genomicdiagnostics.com.au](http://www.genomicdiagnostics.com.au)