The Royal College of Pathologists of Australasia
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Indications for Pharmacogenomic Testing in Australia Project Feedback Form

Name of organisation: Royal Australian and New Zealand College of Psychiatrists (RANZCP)

Reviewer: Dr Elizabeth Moore, President

What is your overall feedback on the Clinical Indications For Pharmacogenomic Testing In Australia project?

The Royal Australian and New Zealand College of Psychiatrists (RANZCP) thanks the Royal College of Pathologists of Australasia (RCPA) for the opportunity to comment on the draft guidelines on clinical indications for pharmacogenetic testing in Australia.

The RANZCP welcomes this RCPA project, funded by Australian Genomics, to develop guidelines on clinical indications for pharmacogenetic testing in Australia. There are few Australian guidelines regarding the indications for pharmacogenetic testing, which has caused a large gap between the local utilisation of pharmacogenetics and what is considered best practice overseas. The RANZCP welcomes this project as a step to address this barrier by outlining the indications for specific drugs. Specifically, the RANZCP welcomes the clarity about the level of evidence for pharmacogenetic testing of psychotropic medications that will be an asset for psychiatrists in relation to their prescribing.

The RANZCP worked with the RCPA in development of, and endorsed, the RCPA statement on utilisation of pharmacogenetics in health care, first released in 2018, which recognises the potential for pharmacogenetic testing in psychiatry where only 50% of patients respond to their initial drug, and there being a prolonged trial and error approach to drug selection and dose.

The RANZCP welcomes the clear information within the guidelines about the role of genes CYP2D6 and CYP2C19, which are primarily responsible for the metabolism of many psychotropic drugs (approximately 1 in 6 people have variations in CYP2D6 that slow drug metabolism, while 1 in 3 have variants in CYP2C19 that accelerate drug metabolism) and how testing for these may impact prescribing.

The guidelines are consistent with the RANZCP Clinical Practice Guidelines for Mood Disorders (2020), and the Royal College of Psychiatrist (UK) guidelines: Personalised prescribing: using pharmacogenomics to improve patient outcomes (2022), that favour testing only in certain difficult to treat depression situations.

The RANZCP further welcomes the proposed 'living' nature of the guidelines whereby the evidence for gene testing will be regularly updated. Precision medicine in psychiatry remains an area of much promise, but one in need of firmer independent RCT data before it can be adopted widely. Inclusion

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of environmental factors, epigenetics through methylation status, and machine learning models may also enhance the clinical utility of the field. The RANZCP welcomes ongoing research in this area, particularly as recent findings suggest that pharmacogenomic testing offers health systems an opportunity for a major value-promoting investment.[1]

The RANZCP recognises that these guidelines will initiate submissions for Medicare Benefit Schedule (MBS) funding of two pharmacogenomic tests: the DYPD gene (to avoid fluoropyrimidine toxicity) and HLA tests (to avoid HLA-related hypersensitivity to carbamazepine) based on the definitive benefits of these tests. The RANZCP would welcome further discussion about the potential for making MBS items available for psychiatric patients to undergo testing for CYP2D6 and CYP2C19 available, especially if a trial of two medications have not provided the desired benefits or are not tolerated so that further choice of the third and subsequent medications could be guided accordingly. This may have benefit in reducing the burden for both patients and for the services from a prolonged trial and error approach.

The RANZCP looks forward to continuing to work with RCPA on matters relating to pharmacogenetics to optimise patient outcomes.

Are the indications categories clear and relevant?

Yes, the RANZCP considers the categories clear and relevant and welcomes the four-tiered approach to recognising the strength of the indication for pharmacogenomic testing:

- Recommended
- Consider
- Available
- No indication identified

Which of the 35 drugs are relevant to your organisation's members?

The drugs most relevant to psychiatrist prescribing sit across the three categories of available, consider, and recommended. The list of relevant drugs are as follows:

Available

- Clomipramine - TCA
- Doxepin – TCA
- Escitalopram – SSRI
- Imipramine – TCA
- Paroxetine – SSRI
- Sertraline - SSRI

[1] Ghanbarian S, Wong GW, Bunka M, Edwards L, Cressman S, Conte T, Price M, Schuetz C, Riches L, Landry G, Erickson D. Cost-effectiveness of pharmacogenomic-guided treatment for major depression. CMAJ. 2023 Nov 14;195(44):E1499-508.

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Consider

- Amitriptyline – TCA
- Atomoxetine - SNRI (ADHD)
- Citalopram - SSRI
- Nortriptyline - TCA

Recommended

- Carbamazepine - anticonvulsant (epilepsy, nerve pain, bipolar disorder when other treatments have failed)
- Oxcarbazepine (derivative of Carbamazepine)

Do you have feedback regarding a specific drug document?

Drug: Carbamazapine

Feedback: The RANZCP notes that this guidance will initiate a submission for Medicare Benefits Schedule (MBS) funding for pharmacogenomic tests for human leukocyte antigens (HLA) to avoid HLA-related hypersensitivity to carbamazepine.

In the RANZCP Clinical Practice Guidelines for Mood Disorders (2020) Carbamazapine is recommended as an alternative option for people with bipolar disorder where choice agents are unavailable, unsuitable or have already been trialled. Monotherapy and combinations of medications are possible and carbamazepine (a mood stabiliser) is marginally more favourable than the antipsychotics ziprasidone, haloperidol and olanzapine, primarily because it is less likely to cause long-term side-effects. In these guidelines, HLA genetic testing in patients of Asian ancestry is advisable prior to initiating carbamazepine to minimise Stevens-Johnson syndrome (SJS) risk. This recommendation is therefore supported.

Once finalised, would your organisation consider endorsing the Clinical indications for pharmacogenomic testing in Australia?

The RANZCP would consider endorsement in line with its Endorsing external or third-party clinical guidance policy.

Do you have any other comments or feedback?

Thank you for consulting with the RANZCP.

Thank you for your feedback; please return your response to rajueln@rcpa.edu.au by **19th December 2023**

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