Professional Practice Guideline 4:

‘Off-label’ prescribing in psychiatry

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The Royal Australian & New Zealand College of Psychiatrists

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Purpose

The Royal Australian New Zealand College of Psychiatrists (RANZCP) has developed this guidance to provide advice to psychiatrists who may be considering the use of medications ‘off-label’, with a key focus on risk identification and justification.

Definitions

‘Off-label’ prescribing refers to the prescription of a registered medicine for a use that is not included in the product information approved by the Australian Therapeutic Goods Administration (TGA) or the New Zealand Medicines and Medical Devices Safety Authority (Medsafe), including when the medication is prescribed or administered for another indication (illness), at a different dose, via an alternative route of administration, for a longer time period, or for a patient of an age or gender outside the registered use.

Regulation

In Australia, therapeutic goods are included in the Australian Register of Therapeutic Goods (ARTG) with either specific indication(s) or intended purpose(s). The *Therapeutic Goods Act 1989* does not regulate clinical practice. 'Off-label’ use is a clinical decision made at the discretion of the treating clinician who is responsible for obtaining informed consent from their patient and ensuring that the therapeutic good is the appropriate treatment option and carries a positive benefit–risk profile.

In New Zealand The Medicines Act 1981 includes provisions that allow for approved medicines supplied outside their approved use. Medsafe has developed information on the unapproved use of medicines. Using an approved medicine in a new or different way requires the prescriber to explain what is being prescribed, and obtain consent. This is required under the Code of Health and Disability Services Consumers' Right.

Prescribers in Australia also need to comply relevant state and territory legislation in regard to use of medicines off-label.

Background

Use of medications outside of TGA or Medsafe approved use does not mean that a medication is ineffective for that circumstance. In some cases, indications identified by regulatory authorities for approved use are more restrictive than the range of conditions or doses for which evidence is available to guide practice. Off-label prescribing is common in psychiatry. [1,2]

The RANZCP supports the quality use of medicines and other treatments and recognises that high levels of off-label prescribing in psychiatry frequently reflect regulatory obstacles to repurposing medications. [3-5] Many evidence-based medications remain off-label owing to sponsors not being financially motivated to apply to have their medications re-purposed.

Medications approved by the TGA or Medsafe are not automatically eligible for third-party payer subsidy (i.e. Pharmaceutical Benefits Schedule (PBS) listing in Australia and Pharmac listing in New Zealand), however medications used outside of approved use are generally ineligible for such subsides meaning that costs are met personally by the patient.

The RANZCP continues to work with relevant organisations to effect policy change to ensure that patients can receive high quality and affordable evidence-based treatments.

Guidance for off-label prescribing in psychiatry

The RANZCP recognises that there are times when a psychiatrist may need to consider the use of off-label prescribing.

There are important clinical and ethical considerations associated with prescribing off-label. [1]

There are inherent risks associated with using medications off-label that need to be considered, recognising that use of some medications off-label is riskier than others. The most common types of off-label prescribing include:

- prescribing where there is strong evidence-base
- prescribing where the evidence base is less but is in line with common clinical practice
- prescribing that may deviate to such an extent from clinical practice and/or lack an evidence base that they are more aptly regarded as experimental.

In every case, psychiatrists should be aware of the full range of treatment options available for the condition they are treating, and be informed by the evidence-base and implications of using medicines off-label. Psychiatrists should be aware of the varying level of risk, align their practice accordingly, and ensure that there is justification for use of medications off-label.

Treatments regarded as experimental should be referred to an appropriate Ethics Committee for advice and review before being instituted.

Patients should be fully informed of these considerations where circumstances apply:

Consent and patient selection

- Prescription of medication off-label should be reserved for those patients where standard treatments have not improved symptoms, or the proposed use of the medication outside the usual range of practice are considered appropriate and necessary.
- Informed consent needs to be obtained and documented in line with Principle 5 of the RANZCP Code of Ethics. The patient may also withdraw consent to the use of off-label medications at any time. It would be appropriate for families and carers to be involved in the consent process depending on the patient's preference.
- The reason(s) for non-standard treatment should be explained to the patient and these reasons clearly and accurately documented in the patient's records along with a thorough assessment of the patient's psychiatric diagnosis and clinical (both mental and physical) state.
- Psychiatrists should use shared decision making to ensure patients are aware when a treatment is being prescribed off-label, what off-label use means, and are informed of the known and unknown benefits and risks. This includes understanding the implications of not having that treatment, and information about alternative treatment options, and furthermore informing patients that they may have to personally meet added costs due to lack of third-party payer subsidy.
- There is a presumption of capacity, regardless of a patient's legal status under mental health legislation, unless evidence is found to the contrary.

- Where a person is found to not have legal capacity to give informed consent, off-label medication should only be prescribed within an appropriate legal framework, which may involve mental health or guardianship legislation or power of attorney.
- Psychiatrists should identify the need for peer review. Some jurisdictions may also require a treating psychiatrist to seek the support of an independent second opinion in relation to the proposed off-label use of medication. Regardless of whether the relevant legal framework requires a second opinion from an independent second psychiatrist, consultation with an experienced colleague should be considered, including potentially a formal written request for a second opinion on treatment options prior to commencing treatment if practical in the circumstances.

Monitoring and outcomes

- Relevant monitoring, including therapeutic serum level monitoring where available, should be undertaken and recorded. Pharmacogenetic testing can be helpful. Appropriate vital signs and other physical signs should be monitored regularly as needed. Clinical progress should be monitored at a frequency appropriate to the patient's mental and physical status.
- The rationale for off-label prescribing, and clinical indicators for a response to the proposed treatment should be documented and discussed with the patient e.g. reduction of target symptoms. Before initiating treatment, the patient's management plan should contain a maximum duration of treatment to be undertaken to assess its benefit and to determine whether the treatment should continue or be ceased. Regular review of the patient and discussion of the patient's progress should be documented, including seeking a second opinion as appropriate. Continuation of the treatment may proceed with documentation of the benefit and specific ongoing review of progress.
- Consistent with the prescription of all medications, any prescription of an off-label medication should include ongoing monitoring of use, outcome and any adverse effects or events. Psychiatrists are encouraged to utilise outcomes data from observational real-world studies to help address evidence gaps where they exist by contributing to clinical registries and by publishing clinical findings.

Professional practice

- As with the use of any medication, off-label prescribing should be in line with RANZCP Position Statement Minimising, and where possible, eliminating the use of seclusion and restraint.
- When psychiatrists are communicating with GPs or other clinicians, it should be clear that the patient has been prescribed an off-label medication, the duration of treatment and any ongoing monitoring requirements that the GP or other clinician should be made aware of.
- Consistent with the prescription of all medications, psychiatrists should ensure that they have appropriate indemnity insurance as required by legislation in Australia or New Zealand, either as an individual or under their organisation's policy prior to prescribing any off-label medication.
- Psychiatrists should be aware of the consequences of using false information to get access to medication.

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Resources and further reading

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REVISION RECORD

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11/1991	1.0	GC1991/02.R35	Adopted
08/2008	2.0	GC2008/03.R32	Updated
02/2016	3.0	B2016/1 R29	Updated and title changed. The original title of the document was: PPG 4: The use of medications in dosages and indications outside of normal clinical practice.
05/2018	3.1	Chair, PPPC	Minor wording revisions to improve clarity of recommendations and to reference the 2018 RANZCP Code of Ethics.

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