Requirements for seeking authorisation to prescribe ketamine for Treatment-Resistant Depression (TRD) in Tasmania

Summary

- Treatment-resistant depression (TRD) is defined as an insufficient response to at least two adequate antidepressant treatments and is associated with low rates of improvement.[1]
- Ketamine is currently approved as an anaesthetic drug by the Therapeutic Goods Administration (TGA) in Australia, but it is not currently approved for use in treating depression. Therefore, the use of ketamine for TRD is an unregistered experimental treatment.
- Whilst emerging research has shown improvement in patients with bipolar depression, most researchers only measured the short-term effects of a single dose of ketamine, therefore the long-term effects of ketamine prescribed in patients with depression are currently unknown.[2] There are still significant gaps in knowledge about dosage levels, treatment protocols and the effectiveness and safety of long-term use.
- Ketamine is listed in Regulation 24 of the *Poisons Regulations 2018*. It is a legal requirement that psychiatrists seek and gain authorisation under Section 59E of the *Poisons Act 1971* before initiating patient treatment with these narcotic substances.
- The authorisation process requires a psychiatrist wishing to prescribe ketamine to provide appropriate and relevant clinical information, demonstrating they have minimised (and adequately counselled the patient on) the risks of harm from the experimental use of ketamine.
- The United States' Food and Drug Administration has approved the use of esketamine intranasally (Spravato™) for TRD. The FDA approval requires patients to be monitored by a health care provider for at least two hours after receiving their Spravato™ dose. There are currently trials underway in Australia for the use of esketamine in TRD.[3]
- These requirements will be subject to review as new clinical practice guidelines become available.

Background

- Ketamine is a narcotic (Schedule 8) substance and is only approved in Australia by the TGA for use as an anaesthetic drug.
- Ketamine has sedative, hallucinogenic, and analgesic properties.

- It induces a state of dissociation, can be misused as a recreational drug, and has addictive, psychosocial effects in humans.
- Ketamine is a common drug of abuse worldwide with the street name 'K' or 'Special K'.[3,4]
- In the past decade, ketamine has emerged as a potential antidepressant.[5,6]
- This has resulted in some clinicians promoting 'off-label' use of ketamine in treating patients with depression.
- The long-term effects of ketamine use in patients with TRD are unknown.[7]

Recommendations from the RANZCP '*Clinical Memorandum Use of ketamine for treatment-resistant depression' (November 2019)*

- The use of ketamine for the treatment of depression is considered a novel treatment. Psychiatrists should provide patients and their carers with clear information and a detailed explanation of the current evidence and potential risks, as well as documenting this in the clinical notes. For more information, refer to the RANZCP '*Professional Practice Guideline 4: 'Off-label' prescribing in psychiatry' (May 2018)*.
- Ketamine should be used under research trial conditions that includes oversight by an institutional research ethics committee and careful monitoring and reporting of effectiveness and safety outcomes.
- Psychiatrists who are considering prescribing ketamine for a patient with TRD, outside a research trial:
    - Should ensure the patient is willing and able to consent.

  AND:
    - Should discuss this treatment with peer(s), preferably including a second opinion, and/or
    - Seek institutional review by a Medicines Advisory Committee or Medicines Assessment Advisory Committee, and/or
    - Seek consideration by an institutional research ethics committee.

Authorisation under Section 59E of the *Poisons Act 1971*

All applications for legal authority to prescribe ketamine for TRD, under Section 59E of the *Poisons Act 1971*, will be referred by the delegate to the Ketamine Advisory Panel (KAP) for assessment and advice. The KAP will consist of specialist psychiatrists and where required, an addiction medicine specialist.

Further information may be requested from applicants to enable the KAP to provide appropriate advice to the delegate. Initial authorities will be for a trial period of three months only.

Subsequent applications will require a detailed report on the patient's progress, including the results of validated screening tools (e.g. Hamilton Depression Rating Scale) to measure and document any symptom change(s).

Part One

Essential requirements for all applications (to be provided to the PSB):

- ☐ The treating clinician (applicant) must hold current registration as a psychiatrist.
- ☐ The patient has been diagnosed with TRD as documented in the *RANZCP clinical practice guidelines for mood disorders*.
- ☐ Informed patient consent form(s) signed by both the patient and the treating psychiatrist.

The applicant must also provide the following supporting documents to PSB for all patients:

- ☐ A comprehensive patient history; including diagnosis, concurrent medications, details of past unsuccessful therapeutic interventions (including pharmacological and psychological).
- ☐ Completed *Ketamine s59E Application* form.
  - Applications for patients who have current or past history of substance misuse disorders must be accompanied by a recent report from an addiction medicine specialist or addiction psychiatrist[Ψ], providing a documented risk assessment and management plan.
- ☐ Detailed supporting information regarding the proposed treatment regimen, including:
  - Proposed treatment regimen, timeframe and treatment goals, including withdrawal protocol in the case of treatment failure.
  - Objective measurements that will inform treatment success or failure.
  - Details of the formulation to be prescribed and the manufacturing facility/pharmacy preparing and dispensing ketamine to patient.

Part Two

Assessment Pathways

Path A - Patient is enrolled in a registered clinical research trial*

The applicant must also provide:

- ☐ A copy of the research protocol and confirmation of institutional ethics committee approval.

Path B – Patient is approved through a Medicines Advisory Committee or Medicines Assessment Advisory Committee**

The applicant must also provide:

- ☐ A copy of the committee approval letter.

All patients being treated for TRD within the Tasmanian Health Service must follow either approval Path A or B.

Path C – Patient not involved in a clinical trial and prescriber not able to access a Medicines Advisory Committee of Medicines Assessment Advisory Committee

The applicant must also provide:

- A written second opinion from a currently registered psychiatrist at the time of application, clearly assessing the risks versus benefits of the proposed regimen.

It should be noted an authority to prescribe is not an endorsement of the need for a particular drug or dose.

[Ψ] Addiction psychiatrist is defined as a psychiatrist who has completed the relevant certificate of advanced training in addiction psychiatry.

** Clinical research trial that includes oversight by an institutional human research or clinical ethics committee*

*** Example includes the Tasmanian Medicines Access and Advisory Committee (TMAAC) for patients of the Tasmanian Health Service.*

These requirements are based on:

1. Legislative requirements for medical practitioners wishing to prescribe narcotic (Schedule 8) substances to seek authorisation under Section 59E of the *Poisons Act 1971* and Regulation 24 of the *Poisons Regulations 2018; and*

2. Recommendations of the Royal Australian and New Zealand College of Psychiatrists (RANZCP) '*Clinical Memorandum Use of ketamine for treatment-resistant-depression' (November 2019).*

References

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4. Sassano-Higgins S, Baron D, Juarez G, Esmaili N, Gold M. A review of ketamine abuse and diversion. Depression and anxiety. 2016;33(8):718-27.
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