SA Palliative Care

Community Pharmacy Update

A joint initiative of South Australian Palliative Care Services

It is useful for Community pharmacists to be aware of Ketamine as it enters the market for new indications as well as it's off-label uses in palliative care patients.

What is Ketamine

Ketamine has primarily been used as an anaesthetic agent via IV injection since it's registration in 1960. Since this time, it's uses off-label for depression, as well as management of acute and chronic pain has increased.

Ketamine is a racemic mixture of two enantiomers, S-ketamine (esketamine) and R-ketamine. Both are *N-methyl-D-aspartate* (NMDA) antagonists, of which esketamine binds more potently. NMDA receptor activation have been associated with hyperalgesia, neuropathic pain and reduced function of opioid receptors.

Ketamine is also an opioid receptor agonist, which may explain it's efficacy for acute pain, being opiate sparing, as well as contributing to anti-depressive effects. It binds to a large variety of receptors.

Esketamine intranasal (Spravato®) has recently been approved for use in treatment resistant depression by the TGA.

Which patients may benefit from using Ketamine?

- > Those with high opioid requirement. Ketamine has an opioid sparing effect
- > Chronic pain.
- > **Intolerance** to other analgesic agents
- > Opioid-Induced Hyperalgesia, (where suspected overactivation and stimulation of the NMDA-receptor has been theorised)

Clinical Considerations

 Adverse effects: Commonly psychotomimetic effects (hallucinations, agitation, anxiety, dysphoria, and euphoria).
May also cause dizziness, nausea, sedation and tachycardia. ADR's are dose dependent.

- Contra-indications: raised intracranial pressure; uncontrolled hypertension, delirium or recent seizures; history of psychosis
- Hepatic impairment May need dose reduction. Significant first pass metabolism. Metabolised by CYP3A4 and CYP2B6. Ketamine infusions have also caused an increase in LFTs.
- Psychiatric conditions (schizophrenia, psychosis, PTSD). Can exacerbate or worsen psychotic symptoms.
- > Cardiac disease; increases cardiac output.
- Drug interactions: Be aware of medications which affect these enzymes can result in changes of ketamine AUC.
- Frail or elderly patients may need smaller doses less frequently
- Potential for abuse; targeted for it's euphoric and dissociative effects. Street named "Special K"

Access Considerations

- > SPRAVATO[™] is registered by the TGA, but not covered by the PBS.
- > Ketamine wafers (Wafermine™) TGA has granted supply under Section 5A of the Therapeutic Goods Act 1989.

Resources

- > TGA: SPRAVATO Product Information
- > Ketamine (Scottish Guidelines)

For more information

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This update is intended to provide practical up to date and factual information relating to pharmacy and medicines management in the setting of Palliative Care and is based on critical review of available evidence. Individual patient circumstances must be considered when applying this information. Please feel free to distribute this update further to interested colleagues.

