Ketamine (Red)*

Introduction

Description

Anaesthetic agent used with specialist supervision as a third-line analgesic to manage complex pain. It is an N-methyl-D-aspartate (NMDA) receptor inhibitor. This use is outside the UK marketing authorisation.

Preparations

(Note: Will need indication for use on prescription, for example ‘for nerve pain’.)

<table>
<thead>
<tr>
<th>Preparation</th>
<th>Details</th>
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<tbody>
<tr>
<td>Ketamine injection</td>
<td>Used by subcutaneous injection/infusion. Specialists occasionally give intravenous (IV) ketamine – see below</td>
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<tr>
<td>Ketamine oral solution</td>
<td>50mg/5ml (unlicensed specials medicine) (This is the preferred strength but other options are available) Injection may be given orally</td>
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</tbody>
</table>

Ketamine is a Schedule 2 CD (Controlled Drug), therefore all prescriptions must satisfy CD prescription requirements to be valid and include details of the dose, form, strength, directions for use and total quantity (in both words and figures). It must also follow CD storage and recording regulations.

Sample prescription

Indications

Unlicensed†

- Neuropathic pain poorly responsive to titrated opioids and oral adjuvant analgesics (for example antidepressant and/or anticonvulsant) particularly when there is abnormal pain sensitivity - allodynia, hyperalgesia or hyperpathia.
- Complex ischaemic limb pain or phantom limb pain.
- Poorly controlled incident bone pain (often has a neuropathic element).
- Complex visceral/abdominal neuropathic pain.

†† Indicates this use is off licence

†QT Indicates this medication is associated with QT prolongation

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Cautions

- Use low doses, carefully monitored, in cardiac failure, cerebrovascular disease, ischaemic heart disease.
- If used for over 3 weeks and there is a need to stop treatment, discontinue ketamine gradually.
- Consider dose reduction in severe hepatic impairment.

Contra-indications

- Do not use ketamine if patient has raised intracranial pressure; uncontrolled hypertension, delirium or recent seizures; history of psychosis.

Drug interactions

- Ketamine interacts with theophylline (tachycardia, seizures) and levothyroxine (monitor for hypertension, tachycardia).
- Diazepam increases the plasma concentration of ketamine.
- Refer to relevant British National Formulary (BNF) section for further information.

Side effects

- Hallucinations, dysphoria and vivid dreams.
- Hypertension, tachycardia, raised intracranial pressure.
- Sedation at higher doses.
- Erythema and pain at infusion site.
- Urinary tract symptoms, for example frequency, urgency, urge incontinence, dysuria and haematuria. (Where is there no evidence of bacterial infection, consider discontinuing ketamine and seeking urology advice.)

Dose and administration

Starting ketamine

- Ketamine is started on the recommendation of a palliative medicine consultant. This is usually done in an inpatient setting.
- Very occasionally, a patient may need to start ketamine in the community. The route of choice is generally oral ketamine. The palliative medicine consultant will liaise closely with the GP, community nurse, and unscheduled care service.
- 24-hour palliative medicine advice will be available.
• Patients starting ketamine will be taking a regular opioid. Ketamine may restore the patient’s opioid sensitivity and lead to opioid toxicity.

• The specialist may recommend changing to a short acting, regular opioid before starting ketamine, particularly if the patient has side effects from the current opioid dose.

• Monitor closely for signs of opioid toxicity (for example sedation, confusion); reduce opioid dose by one third if the patient is drowsy and seek advice.

• Hallucinations/dysphoria. If the patient is not drowsy this is more likely to be a ketamine side effect than due to opioids.

• Give haloperidol oral 500micrograms to 1mg twice daily or SC 1mg to 2mg once daily. Midazolam SC 2mg as needed can also be used.

• Preventing ketamine dysphoria – consider oral haloperidol 500micrograms to 1mg daily when starting ketamine. It can be stopped when the patient’s ketamine dose is stable.

Dose and administration – oral ketamine

• Ketamine can be started using the oral route or patients may be changed from an SC infusion when pain is controlled.

• Starting dose: 5mg to 10mg four times daily.

• Increase dose in 5mg to 10mg increments.

• Usual dose range: 10mg to 60mg four times daily.

Dose and administration – subcutaneous ketamine infusion

• Starting dose: 50mg to 150mg/24 hours.

• Review daily; increase dose in 50mg to 100mg increments.

• Usual dose range: 50mg to 600mg/24 hours (higher doses are occasionally used in specialist units).

Administration

• Prepare a new syringe every 24 hours.

• Dilute ketamine with sodium chloride 0.9%.

• Check the syringe is not cloudy and protect it from light.

• Ketamine stability and compatibility – refer to CME T34 syringe pump ketamine compatibility table in guidelines/on website.

• Dispose of the ketamine vial in accordance with the local policy.
• Rotate the SC infusion site daily to prevent site reactions. If these occur, increase the volume of sodium chloride 0.9% used to dilute the ketamine if possible and/or add a maximum of 1mg of dexamethasone injection to the ketamine infusion.

Converting from a 24-hour SC ketamine infusion to oral ketamine
• Oral ketamine is more potent than SC ketamine (due to liver metabolism). Many patients require a dose reduction of 25-50% when changing to oral ketamine.
• Prescribe the oral ketamine in divided doses - four times daily.
• Titrate dose in 5mg to 10mg increments.
• Some specialists stop the SC infusion when the first dose of oral ketamine is given. Others gradually reduce the infusion dose as the oral dose is increased.

Dose and administration – parenteral ketamine
• Palliative medicine consultants or anaesthetists occasionally administer SC or IV ketamine as single or ‘pulsed’ doses for severe pain or to cover painful procedures.
• Specialists have used IV ketamine infusions to manage ischaemic limb pain.

Practice points

Patient monitoring
• Patients who are at risk of hypertension, tachycardia, respiratory depression or opioid toxicity should only start ketamine in a clinical area able to monitor them 2 to 4 hourly for the first 24 hours.
• All patients should be medically reviewed at least once daily until stable, and then weekly.
• Once the pain is controlled, the palliative medicine specialist may recommend a gradual reduction in the dose of opioid and/or ketamine.

Blood pressure
• Check blood pressure is normal or well controlled before starting ketamine. Record a baseline blood pressure.
• Check blood pressure one hour after the first dose of oral ketamine or starting a SC infusion.
• Check blood pressure 24 hours after the first dose of ketamine, then daily.
• If blood pressure increases 20mmHg above baseline inform the patient’s doctor.
• If blood pressure remains elevated 20mmHg above baseline on repeated measurement, stop the ketamine and seek advice from a palliative medicine specialist.
Pulse
• Record a baseline pulse rate.
• Check pulse one hour after the first dose of ketamine or starting SC infusion.
• Check pulse 24 hours after the first dose of ketamine, then daily.
• If pulse rate increases 20bpm above baseline or rises above 100bpm, inform the patient’s doctor.
• If there is no other cause of tachycardia, seek advice from a palliative medicine specialist.

Respiratory rate
• Record a baseline respiratory rate.
• The palliative medicine specialist will advise on frequency of monitoring.
• If respiratory rate decreases to 10 breaths/minute inform medical staff. Seek advice from a palliative medicine specialist.
• **Naloxone** (in small titrated doses) is only required for reversal of life-threatening respiratory depression due to opioid analgesics, indicated by:
  - a low respiratory rate < 8 respirations/minute
  - oxygen saturation <85%, patient cyanosed.
• Naloxone should not be given in large bolus doses as it can precipitate an acute opioid withdrawal reaction. Refer to *Naloxone* guideline.

Dysphoria, hallucinations, vivid dreams
• Assess patient daily until ketamine dose is stable; then stop any regular CT haloperidol or midazolam.

Patient and carer advice points
• There can be a delay of several days in obtaining further supplies of ketamine. Advise patients to ensure new supplies are requested in adequate time.
• The taste of ketamine can be unpleasantly bitter. Patients can suck or chew on something sweeter after taking. Other flavours can also be requested.

Resources and references


**Stability references**
