Ketamine Palliative Care Shared Care Guideline

Specialist Details	Patient Identifier
Name: _____	
Location: _____	
Tel: _____	**Date:** _____

Introduction

Ketamine is a short acting anaesthetic with analgesic properties at low doses. It is used particularly for neuropathic pain, ischaemic limb pain and refractory cancer pain and as an adjunct to opioid therapy. Ketamine may be given orally or by continuous subcutaneous infusion via syringe pump, either as a sole agent or in combination with other agents. Ketamine for these indications is unlicensed and should only be initiated by a Palliative Medicine Specialist. **Ketamine is a schedule 2 (part 1) controlled drug.**

Adult Dosage and Administration

Dose recommendation varies depending on oral or subcutaneous use and clinical response. Conversion between oral and subcutaneous doses should be managed with specialist palliative care advice.

Oral Ketamine (as 50mg/5mL solution): Start at low doses such as 5-10mg four times daily. The dose can normally be increased in steps of 5-10mg up to a dose of 100mg four times daily. (Higher doses may be used with specialist guidance).

Use caution when calculating volume for administration: Incidents have been reported with oral ketamine as a result of confusion regarding the standard strength, particularly where lower doses are used and the dose is a small volume. For example, a 10mg dose is 1mL of the 50mg/5mL oral solution, 25mg dose is 2.5mL of the 50mg/5mL oral solution. Ensure patients are counselled on measurement of the dose, and use an oral syringe. BNF guidance recommends limiting supply of controlled drugs to 30 days treatment.

Subcutaneous Ketamine: Usual starting dose: 25-50mg over 24hours using a syringe pump and increase by 25mg – 50mg every 24 hours until benefit is achieved. It is unusual to require doses greater than 500mg per day. When given via a syringe pump it can be irritant to the subcutaneous tissue. Dilute with sodium chloride 0.9% to the largest possible volume.

Use caution when calculating volume for administration: Incidents have been reported with subcutaneous ketamine as a result of confusion between the available preparations of ketamine injection.

Suitability in a Syringe Pump

Please seek specialist palliative care advice or refer to www.pallcare.info for information on combinations and compatibilities. Although ketamine is generally incompatible with dexamethasone, small doses of 1mg dexamethasone (as sodium phosphate) or less may be added to syringe pump to prevent site irritation.

Preparations available

Subcutaneous Ketamine: Ketamine vials are available as 10mg/mL (20ml vial) and 50mg/mL (10ml vial). The higher strength 500mg in 10mL may be preferable to allow maximal dilution, room for the addition of other medicines, and reduce irritation, even at doses under 200mg. Orders should be made by contacting Customer Services at (Alliance 03301000448) or Pfizer (01304616161).

Oral Ketamine Solution 50mg/5mL IS THE STANDARD STRENGTH THAT MUST BE USED. It is available to community pharmacists from wholesalers including Rosemont Pharmaceuticals (01132441999), and Sangers Surgical (02890403409). It may take up to 7 working days for delivery. It comes in 300mL bottles; however, other sizes may be available on request. These preparations expire 28 days from opening. Prescribe a total volume proportionate to the daily prescribed dose. **Issue an oral syringe and adapter bung when dispensing**.

Adverse Effects, Precautions and Contraindications

- Intracranial hypertension is an absolute contraindication. Hypertension, cardiac failure, previous cardiovascular events and CVA are relative contraindications. It should be used with caution in seizures.
- Vivid dreams, hallucinations, excessive salivation/secretions, and sedation are the most commonly reported problems. Hypertension and tachycardia can also occur.

- Patients on levothyroxine may be at increased risk of hypertension and tachycardia.
- Concurrent use with other CNS depressants can potentiate CNS depression and/or increase the risk of developing respiratory depression.
- Cases of ulcerative cystitis have been reported with long term use of ketamine.
- Isolated cases of liver injury, including raised liver enzymes and cholestasis have been reported, especially with higher doses.
- If the patient experiences dysphoria or hallucinations, the dose of ketamine should be reduced. If necessary, prescribe the following as an interim measure; midazolam 2mg-5mg subcutaneously 'as required', or haloperidol 500micrograms-1mg orally or subcutaneously 'as required', or lorazepam 1mg orally 'as required' .
- Rarely, the patient can develop a psychosis. Stop ketamine temporarily, treat as above and contact Palliative Medicine Specialist.
- To avoid withdrawal phenomena after long term use, it is preferable to discontinue gradually. The Palliative Medicine Specialist should be contacted to agree dose reductions and to arrange review.
- Ketamine can impair cognitive function and can affect a patient's ability to drive safely.
- Ketamine can be opioid sparing. Monitor for opioid toxicity and it may be necessary to reduce the opioid dose.

Common Drug Interactions

- Diazepam can increase the half-life and prolong the effects of ketamine.
- Grapefruit juice and macrolide antibiotics may increase plasma concentrations of ketamine.
- Plasma concentrations of ketamine may be reduced by carbamazepine, phenytoin, phenobarbital or rifampicin
- When ketamine and theophylline or aminophylline are given concurrently, a clinically significant reduction in the seizure threshold is observed.
- Avoid concomitant use with memantine (increased risk of CNS toxicity).

Palliative Medicine Specialist Responsibilities

- Assess appropriateness of ketamine use, considering any contraindications.
- Provide patient/carer with ketamine patient information leaflet on use, side effects and monitoring.
- Ensure knowledge of patient's blood pressure (BP) history and check BP before initiation.
- Initiate and titrate the dosage regimen, assessing response and side effects.
- Agree shared care with GP including a clear plan for titration and ongoing Specialist Palliative Care follow up.
    - Include baseline Liver Function Tests (LFTs), BP, heart rate and urinalysis
    - Ensure a copy of the shared care guideline is sent to GP.
    - Notify GP of any ongoing monitoring requirements.
    - Patients in the last three to six months of life do not require additional monitoring unless the ketamine dose is increased, or adverse effects emerge.
- Notify Specialist Palliative Care Community Nurse and District Nurse, as appropriate.
- Ensure prescription details and shared care guideline sent to community pharmacist nominated by the patient.
- Provide rapid reassessment in the event of symptoms suggestive of ulcerative cystitis (frequency, urgency, urge incontinence, dysuria, haematuria – not due to a bacterial infection). Consider gradual dose reduction, discontinuation, or referral to Urologist in conjunction with the GP.
- Review response to and continuing appropriateness of ketamine at intervals individualised to patient complexity, sending a written update to the GP. This may be facilitated by the Community Specialist Palliative Care Team.
- Stop the treatment if no longer considered to be appropriate.
- Ensure at least 7 days supply is issued on discharge to ensure continuity of supply in the community.
- **Strength of vial must be stated on the prescription. Strength of oral solution must be 50mg/5mL.**

GP Responsibilities

- Prescribe ketamine as advised by Palliative Medicine Specialist.
- Provide ongoing monitoring as agreed with the Palliative Medicine Specialist.
- Discuss with Palliative Medicine Specialist if symptoms fail to respond / there is need for rapid dose escalation, adverse effects emerge or when a change of administration route or discontinuation may be indicated.
- Consider the possibility of ulcerative cystitis if the patient develops significant urinary symptoms (frequency, urgency, urge incontinence, dysuria, haematuria – not due to a bacterial infection). Discuss the patient promptly with the Palliative Medicine Specialist.
- **Strength of vial must be stated on the prescription. Strength of oral solution must be 50mg/5mL.**

Communication

For any queries relating to this patient's treatment with ketamine, please contact the Palliative Medicine Specialist named at the top of this document.

This information is not inclusive of all prescribing information and potential adverse effects. Please refer to the full prescribing data SPC, the BNF and the current Palliative Care formulary. Information is also available at www.pallcare.info .

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