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. The dose of opioid may need to be reduced when ketamine is initiated. 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 currently schedule 4 (part 1) controlled drug. (Under review)

Adult dosage and administration
Dose recommendation varies depending on oral or subcutaneous use and clinical response**.**
Conversion between oral or subcutaneous should be managed under specialist palliative advice.

Oral Ketamine (as 50mg/5mL): Start at low doses such as 10-25mg three to four times daily. The dose and frequency can normally be increased in steps of 10-25mg up to a dose of 50mg 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.

Subcutaneous Ketamine: Start with 50-100mg over 24hours using a syringe pump and increase by 50mg increments every 24hours 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
Ketamine normally mixes well depending on concentration with diamorphine or morphine or oxycodone or haloperidol or metoclopramide or levomepromazine or midazolam in a syringe pump. **Ketamine is incompatible with cyclizine**. Ketamine is generally incompatible with dexamethasone but doses of 1mg dexamethasone (as sodium phosphate) or less may be added to syringe pump to prevent site irritation.
If more than two drugs are to be mixed in the same syringe please refer to the current Palliative Care Formulary www.pallcare.info or www.palliativedrugs.com or seek further specialist advice.

Available as

Preparations available: Subcutaneous Ketamine: Ketamine vials are available as 10mg/mL (20mL vial), 50mg/mL (10mL vial),100mg/mL (10mL vial). Orders should be made by contacting Customer Services at Pfizer (0845 6088866) or through Sangers Belfast (028 9040 4070).

Oral Ketamine Solution 50mg/5mL IS THE STANDARD STRENGTH THAT MUST BE USED. This is prepared on request. It is available to community pharmacists from wholesalers including Rosemont Pharmaceuticals (0800 919312**),** Martindale Pharmaceuticals (0800 137627) and Sangers NI (028 90401111). It may take up to 7 working days for delivery. It comes in a variety of flavours e.g. natural (aniseed) and peppermint, and in various sizes including 250mL, 300mL and 500mL. Note these preparations have no preservative and expire 28 days from opening. Please issue an oral syringe and adapter bung when dispensing. **Use caution when calculating volume for administration.**

Palliative Medicines Specialist Responsibilities

- Assess appropriateness of ketamine use, considering any contraindications.
- Provide patient/carer with relevant information on use, side effects and need for monitoring of medication.
- 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 when patient is managed on a stable regimen.
  - Include baseline Liver Function Tests (LFTs), BP ,urinalysis and Heart Rate
  - Ensure a copy of the shared care guideline is sent to GP.
  - Arrange BP check 1-2 weeks into treatment, on dosage increases, and periodically while on treatment.
  - If syringe driver required notify specialist nurses and community nurses.
- Ensure prescription details and shared care guideline is sent to the community pharmacist nominated by the patient.
- 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.**
- For patients on longer term treatment; at review arrange LFTs, and assess patients for symptoms suggestive of ulcerative cystitis.
- 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 or discontinuation or referral to Urologist.
- Review the patient's response and continuing appropriateness of ketamine at specified intervals, sending a written summary to the GP. This may be facilitated by Community Specialist Palliative Care Team.
- Provide any other advice or information for the GP if required.
- Stop the treatment when no longer considered to be appropriate.

GP Responsibilities

- Prescribe ketamine and arrange any on-going monitoring as agreed with the specialist. If advised, monitor LFTs and BP in liaison with specialist.
- **Strength of vial must be stated on the prescription. Strength of oral solution must be 50mg/5mL.**
- Support BP monitoring in community in liaison with Palliative Medicines Specialist: 1-2 weeks into treatment, on dosage increases, and periodically while on treatment.
- Review the patient at regular agreed intervals to monitor control of symptoms.
- Refer to specialist when symptoms fail to respond or when change of administration route 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). Re-refer / discuss the patient promptly with the Palliative Medicines Specialist.
- Liaise with community and specialist nurses.

Adverse Effects, Precautions and Contraindications

- Intracranial hypertension and seizures are absolute contraindications. Hypertension, cardiac failure, previous cardiovascular events and CVA are relative contraindications.
- Patients on levothyroxine may be at increased risk of hypertension and tachycardia.
- Vivid dreams, hallucinations, excessive salivation/secretions, and sedation are the most commonly reported problems. Hypertension and tachycardia can also occur.
- Cases of ulcerative cystitis have been reported with long term use of ketamine.
- Isolated cases of liver injury have been reported, especially with higher doses.
- Rarely the patient can develop a psychosis. If the patient experiences dysphoria or hallucinations, the dose of ketamine should be reduced. If necessary midazolam or haloperidol should be prescribed as an interim measure e.g. 2.5-5mg midazolam subcutaneously or 1.5-5mg haloperidol orally or subcutaneously.
- 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.

Common Drug Interactions

- Plasma concentrations of ketamine may be increased by diazepam.
- 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).
- Grapefruit juice may increase plasma concentrations of oral ketamine.

Communication

For any queries relating to this patient's treatment with ketamine, please contact the 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 or www.palliativedrugs.com

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