Patient Name:
Address:
DOB:
NHS No:
GP:

Sue Ryder
Royal Berkshire NHS
NHS Foundation Trust
Berkshire West NHS
Primary Care Trust

KETAMINE for refractory pain:
SHARED CARE PROTOCOL

Produced by: Paul Howard, Consultant in Palliative Medicine
Authorised by: Berkshire West CHQPSG
Date: May 2010 (oral ketamine preparation details updated May 2011)
Review date: May 2013

This shared care protocol is produced to support the combination of the best of both primary and secondary care for the benefit of the patient. It supports, but does not replace, discussion and agreement on an individual patient basis about transfer of care. Agreement by the GP should be confirmed (verbal or written) before transfer of care.

Responsibilities for care and clinical monitoring

Consultant responsibilities	
Initiation	• Initial assessment of appropriateness of ketamine • Informed consent to start ketamine • Baseline observations and tests • Initial dose titration, including adjusting concurrent analgesia as needed
Prescribing	• Prescription of ketamine during initial dose titration • Prescription of further 14 days of ketamine once stable dose achieved and shared care agreed
Monitoring	• To arrange a named pain or palliative care team member (physician or nurse specialist) to lead ongoing monitoring of efficacy and tolerability • To adjust dose where required • To arrange additional timely re-assessment if the GP raises concern
Communication	• To discuss shared care arrangement with GP and send a copy of this document (including completed clinical summary page) • To inform GP of outcome of re-assessments • To provide 24hr advice (via on-call palliative care consultant or anaesthetist as appropriate)
General Practitioner responsibilities	
Initiation	• None
Prescribing	• Prescription of ketamine once the patient is established on an effective dose and shared care has been agreed (the back page 'pharmacist information' can be torn off and sent with the FP10)

Monitoring	• To consider ketamine as a cause of unexplained:
	  ◦ neuropsychiatric symptoms (e.g. delirium, psychosis)
	  ◦ culture-negative urinary symptoms (e.g. haematuria, dysuria)
	  ◦ altered LFTs (GPs do not need to routinely monitor LFTs, but should consider ketamine as a possible cause of LFTs derangement)

Communication	• To inform the specialist of concerns about inadequate pain control or adverse effects

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Summary of the clinical condition

(The specialist completes the summary section below, including advice for a particular patient that differs to the standard shared care arrangements. Copies of the entire shared care document, including this summary, are kept in the clinical notes, sent to the GP and offered to the patient)

- **Diagnosis**
    - Underlying disease:
    - Pain mechanism (e.g. neuropathic pain):
- **Current regimen**
    - Dose:
    - Frequency:
    - Route:
    - Brand and strength of preparation:
    - Date initiated:
    - Date current regimen reached:
- **Relevant co-morbidities, abnormal baseline observations or tests, or other factors relevant to the use of ketamine**:

When GP could assume responsibility

- The patient has been initiated on the treatment by a consultant in pain or palliative medicine and it is considered clinically appropriate to transfer care.

AND

- shared care has been agreed in accordance with these guidelines between the consultant and the GP

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Appendix 1: How to obtain supplies in the community

We advise patients to order repeat supplies several days in advance to allow the community pharmacist time to obtain the medication.

1. Action Required by the GP - prescribing on FP10 form

Ketamine is a Schedule 4, part 1 Controlled Drug. Usual CD prescription writing requirements **do not apply**. The quantity of drug does not have to be stated in words and figures. ***The pharmacist information is duplicated on the back page so that it can be torn off and taken with the FP10***.

2. Action Required By The Pharmacist

Oral treatment

Huddersfield Royal Infirmary Pharmacy Manufacturing Unit produces an unlicensed oral solution at a concentration of 50mg/5ml. They make this as a batch product in a 100ml size, which needs to be kept in a refrigerator and is flavoured with peppermint and anise. It has a one month expiry once open. This is available through Oxford Pharmacy Stores (tel: 01865 321085 fax: 01865 321090). OPS can supply community pharmacists direct once an account is set up with them.

Injectable preparation for subcutaneous use Ketalar™

Contact Pfizer customer services (Tel: 01304 645262, Fax: 01304 655885) to request a supply. To initiate the supply, Pfizer require the following details to be faxed to them on headed notepaper:

- patient's name
- dose of ketamine prescribed
- quantity required
- GP and pharmacist's details
- details of the pharmacist's local wholesaler (branch and account number)

Depending on the quickest and most convenient arrangement for the pharmacy, Pfizer will then either:

- supply via the local wholesaler or
- supply the pharmacy directly but bill via the wholesaler.

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Appendix 2: pharmacology, background information, common problems

Indication

Ketamine is used for pain refractory to usual measures (e.g. opioids combined with anti-epileptics and tricyclic antidepressants). It reduces the hyperexcitability (central sensitisation) sometimes responsible for refractory pain by blocking NMDA-glutamate receptors. It is widely prescribed by Specialist Palliative Care and Pain teams in Great Britain - further information may be obtained from:

- The pain or palliative care team
- Palliative Care Formulary 3rd Edition. Twycross *et al* 2007, Radcliffe Medical Press
- www.palliativedrugs.com (registration for access is free for health professionals)

Licensing status

One of two preparations is used, depending on the route:

- **Oral:** an unlicensed ketamine 50mg/5ml oral suspension, available from Huddersfield Royal Infirmary Pharmacy Manufacturing Unit via Oxford Pharmacy Stores, is used because the risk of dose and administration errors is lower than with oral use of the parenteral 'Ketalar' preparation.
- **Subcutaneous:** Ketalar™ is used for patients requiring subcutaneous ketamine. This is an off-label indication and off-label route. Care is needed when prescribing/supplying as three strengths are available. The 50mg/ml strength is suggested as the most appropriate for use in a syringe driver, as each vial can be used only once.

Dose and administration

Patients are typically commenced on 10-25mg t.d.s. PO (0800, 1300 and 2200 hrs) and this dose is titrated up every few days by an increment of 5-25mg per dose (5mg = 0.5ml). Patients and their carers are shown how to draw up the volume of solution using oral syringes.

Oral to subcutaneous conversion

Temporary loss of oral route

If a patient temporally loses the oral route, ketamine is normally omitted and re-started orally once the oral route is regained. The analgesic benefit usually persists for a few days beyond discontinuation so pain control is maintained. If in doubt, or if pain starts to recur, discuss initiating subcutaneous ketamine with their pain or palliative care consultant.

Permanent loss of oral route (e.g. at the end of life)

Discuss with the pain or palliative care consultant. If required, subcutaneous ketamine is given:

- via 24 hour subcutaneous syringe driver
- At a dose equal to previous 24 hour oral dose:
  - E.g. ketamine 25mg t.d.s. PO would be equivalent to 75mg over 24hrs via syringe driver
  - This dose can be rounded up or down (+/-10% approx) if needed for ease of administration
- Ketamine can be combined with a small number of other drugs including:
  - **Two drug combinations**. Ketamine plus
    - *one of*: haloperidol, metoclopramide, midazolam, morphine sulphate, oxycodone, or diamorphine
  - **Three drug combinations**. Ketamine plus
    - *one of*: oxycodone, diamorphine or morphine sulphate *plus*
    - *one of*: haloperidol or midazolam
  - For information about other combinations, discuss with the pain or palliative care team
- **Sodium chloride 0.9%** should be used as a diluent,

Adverse effects include:

- **Psychotropic** (derealisation, depersonalisation, hallucinations – usually during initiation or after dose increases. Treated with benzodiazepines and antipsychotics)
- **Cardiovascular** (hypertension, tachycardia – generally mild and identified during initial titration)
- **Urological** (haematuria and dysuria due to chemical cystitis is reported – d/w culture-negative urinary symptoms with pain or palliative care consultant. The incidence is unclear. If unrecognised, fibrosis and obstructive uropathy can eventually occur)
- **Altered LFTs** (generally asymptomatic. Monitor initially. If worsening or severe, discuss further investigation with the pain or palliative care consultant)

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Appendix 3. Pharmacist information

(please detact this page and ask the patient to take it along with the FP10 to their community pharmacist)

Sue Ryder
Royal Berkshire NHS Foundation Trust
Berkshire West Primary Care Trust

Dear pharmacist,
This patient is receiving ketamine for refactory pain. This has been initiated by a specialist in pain or palliative medicine. Please find information below to facilitate its supply.

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