

**South East London Area Prescribing Committee
Formulary recommendation**

Reference	038
Intervention:	Ketamine oral solution (50mg/5ml) for complex pain in palliative care (Ketamine is an anaesthetic agent with broad pharmacological activity including NMDA antagonism).
Date of Decision	September 2015
Date of Issue:	October 2015
Recommendation:	RED – suitable for prescribing and supply by hospital only
Further Information	<ul style="list-style-type: none"> • Ketamine oral solution (50mg/5ml) may be considered for use in the management of complex pain in patients under the palliative care team where ALL the following apply: <ul style="list-style-type: none"> - For any disease that is characterised by hyperalgesia - where a patient experiences an exaggerated response to a painful stimulus that suggests an underlying involvement of the NMDA receptor AND - Where the patient's pain is complex and there are signs that suggest inflammation and/or nerve compression/damage is playing a part in this (for example, post-irradiation damage, tumour breakdown such as fungating breast) AND - Where the patient's pain has not responded adequately to or they have not tolerated standard drug treatments, including optimal use of opioids, non-opioids and co analgesics AND - Generally the patient has a prognosis of more than 4 weeks (as any benefit of therapy with oral ketamine may take up to this length of time to become apparent). • There is currently no licensed preparation of ketamine oral solution in the UK - the preparation is available as an unlicensed special. Patients will need to be informed of this before treatment in line with the organisation's usual consent processes. • The palliative care team will prescribe in line with their Trust's clinical guideline and prescribing of ketamine oral solution will be restricted to named palliative care consultants. • In view of the specialist nature of the drug and the risks involved, prescribing will not be transferred to primary care. • Ketamine will be used at a dose of 15mg to 50mg three times a day, although doses up to 60mg four times a day may be required depending on dose/tolerance.
Shared Care/ Transfer of care required:	N/A
Cost Impact for agreed patient group	It is estimated that there will be approximately 2 patients per 100,000 population suitable for treatment with ketamine oral solution per year (or 36 patients in SEL). Assuming an average dose of 30mg three times a day, this would cost £600 per patient per annum*. This will result in a total approximate cost impact across SEL of £21,600 per year. As ketamine is an in-tariff drug, funding will need to be confirmed at individual Trust level. * based on Trust acquisition costs for the drug

Usage Monitoring & Impact Assessment	<p>Acute Trusts:</p> <ul style="list-style-type: none"> • Monitor usage on a 6-monthly basis • Audit compliance with clinical guideline and report back to APC upon request <p>CCGs:</p> <ul style="list-style-type: none"> • Monitor epect data • Monitor reports from GP practices where transfer of prescribing to primary care is requested.
Evidence reviewed	<p>References (from evidence evaluation)</p> <ol style="list-style-type: none"> 1. Guidance on the provision of anaesthetic services for Chronic Pain Management. The Royal College of Anaesthetists 2009. 2. NICE TAG 159 - Spinal cord stimulation for chronic pain of neuropathic or ischaemic origin. October 08 3. NICE Clinical Guideline 173 - The pharmacological management of neuropathic pain in adults in non-specialist settings. Last Modified December 2014. 4. SIGN Guideline 106 – Control of Pain in Adults with Cancer. November 2008. 5. Hardy J, Quinn S, Fazekas B et al. Randomised, Double-Blind, Placebo-Controlled Study to Assess the Efficacy and Toxicity of Subcutaneous Ketamine in the Management of Cancer Pain. Journal of Clinical Oncology 2012, Vol 30 (29) p3611-3617. 6. Colvin L, Forbes K, Fallon M. Difficult Pain. British Medical Journal 2006, 332(7549) p1081-3. 7. Bell R, et al Ketamine as an adjuvant to opioids for cancer pain (review) 2012. (Cochrane Library) 8. SPC Ketalar 10mg/ml injection. Available here at: <accessed on 23/08/2015> 9. NICE ESMN: Unlicensed or Off-Label Medicine 27 – Chronic Pain Ketamine updated 06/14 10. Mercadante S, Arcuri E, Tirelli W et al. Analgesic effect of intravenous ketamine in cancer patients on morphine therapy: a randomised, controlled, doubleblind, crossover, double-dose study. HJournal of Pain and Symptom Management 2000, 4 p246-252. 11. Yang 1996. Intrathecal ketamine reduces morphine requirement in patients with terminal cancer pain. Canadian Journal of Anaesthesia 1996, 43 (4) p379-383. 12. Lauretti G, Lima I, et al. Oral ketamine and transdermal nitroglycerin as analgesic adjuvants to oral morphine therapy for cancer pain management. Anesthesiology 1999, 90 p1528-1533. 13. Blonk M, Koder B, van den Bemt et al. Use of oral ketamine in chronic pain management: a review. European Journal of Pain 2009, doi 10.1016/j.ejpain.2009.09.005 14. Rabben T, Skjelbred P Oye I. Prolonged analgesic effect of ketamine, an N-methyl-D-aspartate receptor inhibitor in patients with chronic pain. The Journal of Pharmacology and Experimental Therapeutics 1999, 289 p1060-1066. 15. Furuhashi-Yonaha A, Iida H, Takeda A et al. Short and long term efficacy of oral ketamine in eight chronic pain patients. Canadian Journal of Anaesthesia 2002, 49 p886-887. 16. Haines D, Gaines S. N of 1 randomised controlled trials of oral ketamine in patients with chronic pain. Pain 1999, 83 p283-287. 17. MacKintosh D. Ketamine and cancer pain – an inconvenient truth? Annals of Palliative Medicine 2012, 1 (3) DOI:10.3978/j.issn.2224-5820.2012.10.12 18. Advisory Council on the Misuse of Drugs. Ketamine :A review of Use and Harm. 10.12.13. 19. Chong C, Shug S, Page-Sharp M. Bioavailability of Ketamine After Oral or Sublingual Administration. Pain Medicine 2006, 7 (5) p469. 20. Enarson M, Hays H, Woodroffe M. Clinical experience with oral ketamine. Journal of Pain and Symptom Management 1999, 17 p384-386 21. Cvrcek P. Side effects of ketamine in the long term treatment of neuropathic pain. Pain Medicine 2008, 9 p252-257 22. The Drug Tariff August 2015

NOTES:

- a) Area Prescribing Committee recommendations and minutes are available publicly on member CCG websites.
- b) This Area Prescribing Committee recommendation has been made on the cost effectiveness, patient outcome and safety data available at the time. The recommendation will be subject to review if new data becomes available, costs are higher than expected or new NICE guidelines or technology appraisals are issued.
- c) **Not to be used for commercial or marketing purposes. Strictly for use within the NHS.**