

## DORSET MEDICINES ADVISORY GROUP

### COMMISSIONING STATEMENT ON THE USE OF ORAL KETAMINE FOR TREATING CHRONIC PAIN IN CHILDREN, YOUNG PEOPLE OR ADULTS.

#### SUMMARY

Dorset Medicines Advisory Group does not recommend the use of oral ketamine for treating chronic pain in children, young people or adults.

BACKGROUND	<p>Ketamine is an anaesthetic agent. Its analgesic effect is primarily based on the antagonism of the N-methyl-D-aspartate (NMDA) receptor. Activation of NMDA receptors may play a crucial role in the pathogenesis of chronic pain. It has been used to manage very complex pain. Little formal research has been performed on the efficacy and safety of ketamine in chronic pain, especially concerning long-term oral administration.</p> <p>Ketamine (Ketalar®) is not licensed in the UK for treating chronic pain in children, young people or adults. Oral liquid preparations of ketamine are not licensed in the UK, so use of these preparations, which are prepared by 'specials' manufacturers, is unlicensed. Ketamine solution for injection or infusion used orally is an off-label use.</p> <p>Ketamine is controlled as a class C drug under the Misuse of Drugs Act 1971, and as a schedule 4, part 1 drug under the Misuse of Drugs Regulations 2001. The Advisory Council on the Misuse of Drugs has recommended that ketamine be upgraded to class B. This is expected to take effect in June 2014 subject to Parliamentary approval. After reclassification, ketamine will remain a Schedule 4 Part 1 drug until a decision is made, after the public consultation, on the appropriate schedule in which it should be listed.</p>
RELEVANT NICE GUIDANCE	<p>The use of oral ketamine for chronic pain has not been considered for guidance by NICE. It is not currently planned into any other work programme.</p> <p>A NICE evidence summary: unlicensed or off-label medicine for oral ketamine concluded that there is no good quality evidence for the use of oral ketamine to treat chronic pain in adults or children. In the studies that reported safety, oral ketamine was frequently associated with adverse effects that often resulted in treatment discontinuation.</p>
FORMULARY STATUS	Not recommended
PbR STATUS	Not relevant
COMMISSIONING IMPLICATIONS	Not relevant
RELEVANT CLINICAL COMMISSIONING PROGRAMME	General Medical and Surgical

<b>PATIENT PATHWAY IMPLICATIONS</b>	<p>NICE clinical guideline on pharmacological management of neuropathic pain recommends amitriptyline (off-label use), duloxetine (licensed use for diabetic peripheral neuropathic pain), gabapentin (licensed use for peripheral neuropathic pain) or pregabalin as first-line pharmacological treatment for people with neuropathic pain (excluding trigeminal neuralgia). Carbamazepine is recommended as initial treatment for people with trigeminal neuralgia.</p> <p>SIGN (Management of Chronic Pain) recommends ketamine as one option of Step 6 in the Chronic Pain Pathway, restricted to a tertiary drug for specialist referral.</p> <p>SIGN (Control of Pain in Adults with Cancer) advises that the use of ketamine as an analgesic should be supervised by a specialist in pain relief or a palliative medicine specialist.</p> <p>A dose-ranging phase II RCT of oral ketamine for treating chronic pain in children and young people (age range 8 to 20 years) (Ketamine in Chronic Kid's Pain [KiCK Pain]) is recruiting participants and has an estimated completion date of May 2017.</p>
<b>SUMMARY OF EVIDENCE TO SUPPORT FORMULARY STATUS</b>	<p>An independent review states: Evidence on the effect of oral ketamine in chronic pain is limited and the quality of the studies is not very high. The majority of the included studies were non-comparative trials or case reports. The evidence that is available shows that chronic pain patients can have limited benefit from the use of oral ketamine.</p> <p>Oral ketamine for chronic pain has not been assessed by the Scottish Medicines Consortium (SMC) or the All Wales Medicines Strategy Group (AWMSG).</p> <p>The summary of product characteristics states that ketamine is not indicated nor recommended for long-term use as it is associated with serious adverse effects. Cases of cystitis, including haemorrhagic cystitis, have been reported in people being given ketamine on a long-term basis.</p> <p>The Advisory Council on the Misuse of Drugs (ACMD) has highlighted evidence of chronic toxicity to the bladder. There is good evidence that frequent and heavy ketamine misuse can cause significant toxicity to the bladder, urinary tract and kidneys. This can be associated with severe and disabling symptoms that include pain on passing urine, frequency and urgency of urination, blood in the urine and incontinence. Whilst these changes can be reversible with ketamine cessation, there are numerous reports of individuals having to have surgery to remove their bladders because of severe ketamine related bladder damage.</p>
<b>ASSESSMENT OF COST IMPLICATIONS</b>	No studies on the cost effectiveness of oral ketamine for treating chronic pain were identified.

	<p>The NHS Electronic Drug Tariff (January 2014) lists the following prices for ketamine oral solution or suspension:</p> <p>Ketamine 50 mg/5 ml oral solution: £215.90 for minimum volume of 200 ml plus £0.01 for each extra ml.</p> <p>Ketamine 50 mg/5 ml oral suspension: £132.25 for minimum volume of 200 ml plus £0.01 for each extra ml.</p> <p>No price is listed for other strengths of liquid formulation, and the cost of these will differ depending on the source.</p> <p>MIMS (January 2014) lists the following costs for Ketalar®:</p> <p>10 mg/ml, 1×20 ml vial=£5.06.</p> <p>50 mg/ml, 1×10 ml vial=£8.77.</p> <p>100 mg/ml, 1×10 ml vial=£16.10.</p>
	<p>ESUOM27: Chronic pain: oral ketamine Published 25 February 2014, (last updated: 17 March 2014)</p> <p><a href="http://publications.nice.org.uk/esuom27-chronic-pain-oral-ketamine-esuom27/key-points-from-the-evidence#summary">http://publications.nice.org.uk/esuom27-chronic-pain-oral-ketamine-esuom27/key-points-from-the-evidence#summary</a></p> <p>Scottish Intercollegiate Guidelines Network SIGN 136 Management of Chronic pain. December 2013</p> <p><a href="http://www.sign.ac.uk/pdf/SIGN136.pdf">http://www.sign.ac.uk/pdf/SIGN136.pdf</a></p> <p>Scottish Intercollegiate Guidelines Network SIGN 106 Control of pain in adults with cancer November 2008.</p> <p><a href="http://www.sign.ac.uk/pdf/SIGN106.pdf">http://www.sign.ac.uk/pdf/SIGN106.pdf</a></p> <p>Blonk MI et al. Use of oral ketamine in chronic pain management: A review. Eur J Pain (2009), doi:10.1016/j.ejpain.2009.09.005  <a href="file:///C:/Documents%20and%20Settings/katie%20taylor/Desktop/Abstral/Blonk_Koder_et.al.pdf">file:///C:/Documents%20and%20Settings/katie%20taylor/Desktop/Abstral/Blonk_Koder_et.al.pdf</a></p>
REFERENCES	<p>Summary of Product Characteristics. Ketalar 10 mg/ml Injection Pfizer Ltd. Accessed on 24<sup>th</sup> March 2014</p> <p><a href="http://www.medicines.org.uk/emc">www.medicines.org.uk/emc</a></p> <p>Iversen L, Dargan P. for the ACMD Ketamine Working Group. Advisory Council for the Misuse of Drugs. Ketamine: a review of use and harm December 2013</p> <p><a href="https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/264677/ACMD_ketamine_report_dec13.pdf">https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/264677/ACMD_ketamine_report_dec13.pdf</a></p> <p><b>Decisions from adjacent CCGs</b></p> <p>Somerset CCG - Not listed.</p> <p><a href="http://www.sompar.nhs.uk/content/26210/36491/Formulary_15th_Ed_19-3-2013.pdf">http://www.sompar.nhs.uk/content/26210/36491/Formulary_15th_Ed_19-3-2013.pdf</a></p> <p>West Hampshire CCG (Basingstoke, Southampton and Winchester District Prescribing Committee (DPC) – Not listed.</p>

	<p><a href="http://www.westhampshireccg.nhs.uk/documents/cat_view/84-medicines/90-formularies">http://www.westhampshireccg.nhs.uk/documents/cat_view/84-medicines/90-formularies</a></p> <p>Bath Clinical Area Partnership (BCAP) not listed  <a href="http://www.banesccg.nhs.uk/sites/default/files/14TH_Edition_of_BCAP_JF_May_2013.pdf">http://www.banesccg.nhs.uk/sites/default/files/14TH_Edition_of_BCAP_JF_May_2013.pdf</a></p> <p>Northern, Eastern and Western Devon CCG Joint Formulary  <a href="http://www.newdevonccg.nhs.uk/who-we-are//medicines-and-treatments/joint-formularies/100802">http://www.newdevonccg.nhs.uk/who-we-are//medicines-and-treatments/joint-formularies/100802</a></p> <p>North Devon PCT (GP) Formulary - not listed.  Exeter and East Devon Formulary – Only after specialist advice.  The Plymouth Area Joint Formulary – not listed.</p>
<b>Date</b>	March 2014
<b>Review date</b>	March 2016
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