Position statement - Nefopam

ELMMB does not support the prescribing of nefopam tablets and it is assigned a BLACK Traffic Light

- **Nefopam** is a centrally acting non-opioid analgesic with associated antimuscarinic and antihistaminergic effects recommended for persistent pain unresponsive to other non-opioid analgesics.[1]
- The **BNF** indicates nefopam may have a place in the relief of persistent pain unresponsive to other non-opioid analgesics, but prescribers need to consider carefully whether the anticipated benefits outweigh the risks of adverse effects, especially in high risk groups including the elderly.
- Most of the **studies** assessing the efficacy of nefopam are either single dose or short term based; the majority of these involve parenteral administration which is not supported by the UK marketing authorisation. The **evidence base** for the efficacy of nefopam is **weak, conflicting or absent**[2,3,4,5] in reducing pain in patients with RA or postoperative period.
- **Adverse effects are common** and include nausea, sweating, dizziness, vomiting, hallucinations, confusion, urinary retention, headache, insomnia, tachycardia, palpitations convulsions and anaphylaxis
- Nefopam scores 2 on the **anticholinergic burden** scale (ACB).[6] Each definite anticholinergic may increase the risk of cognitive impairment by 46% over 6 years. For each point increase in the ACB total score, a decline in MMSE score of 0.33 points over 2 years has been suggested. Additionally, each one point increase in the ACB total score has been correlated with a 26% increase in the risk of death.
- Nefopam is **toxic in overdose** with observed clinical manifestations including seizures, first degree heart block, right bundle branch block, ventricular tachycardia, acute renal failure, cerebral oedema and pulseless electrical activity. Four deaths following intentional nefopam overdose have been reported. The fatal dose, known in one case only, was 1.8g.
- Nefopam has **abuse potential** primarily through its psychostimulant-like effects, which are probably linked to its dopamine reuptake inhibition properties. There are reports it is being identified on drug screening results. Where nefopam has been used for its abuse potential withdrawal may lead to depression,[7]
  If withdrawn abruptly, anticholinergic agents can cause a discontinuation syndrome, characterised by rebound EPSE, cholinergic rebound, myalgia, depression, anxiety, insomnia, headaches, gastric intestinal distress, nausea, vomiting and malaise. Following chronic use it may be prudent to withdraw slowly and gradually over at least 1-2 weeks

Bottom line what does this mean in practice?
- don't initiate nefopam for acute or chronic pain
- do not continue nefopam post discharge following secondary care acute initiation
- **-review existing patients – assess benefits versus adverse effects and consider stopping; withdraw slowly over 1-2 weeks following chronic use.**

[1] SAFER MEDICATION USE Nefopam No 14 January 2015 RDTC
[2] Richards BL, Whittle SL, Buchbinder R. Neuromodulators for painmanagement in rheumatoid arthritis. Cochrane Database of Systematic Reviews 2012, Issue 1.
[3] Moore RA, Derry S, Aldington D, Wiffen PJ. Single dose oral analgesics for acute postoperative pain in adults - an overview of Cochrane reviews. Cochrane Database of Systematic Reviews 2015, Issue 9.
[4] KakkarM, Derry S, Moore RA, McQuay HJ. Single dose oral nefopamfor acute postoperative pain in adults. Cochrane Database of Systematic Reviews 2009, Issue 3.
[5] Nefopam for the Prevention of Postoperative Pain: Quantitative Systematic Review M. S. Evans; C. Lysakowski; M. R. Tramèr Br J Anaesth. 2008;101(5):610-617.
[6] Aging Brain Care 2012 Update Developed by the Aging Brain Program of the Indiana University Center for Aging Research, See http://www.agingbraincare.org/uploads/products/ACB_scale_-_legal_size.pdf
[7] Villier C, Mallaret MP. Nefopam abuse. Ann Pharmacother. 2002 Oct;36(10):1564-6.

Acknowlegement - North Tyneside CCG 'NTCCG position statement on nefopam' July 2016