

Hartlepool & Stockton-on-Tees CCG and South Tees CCG Position Statement on Nefopam

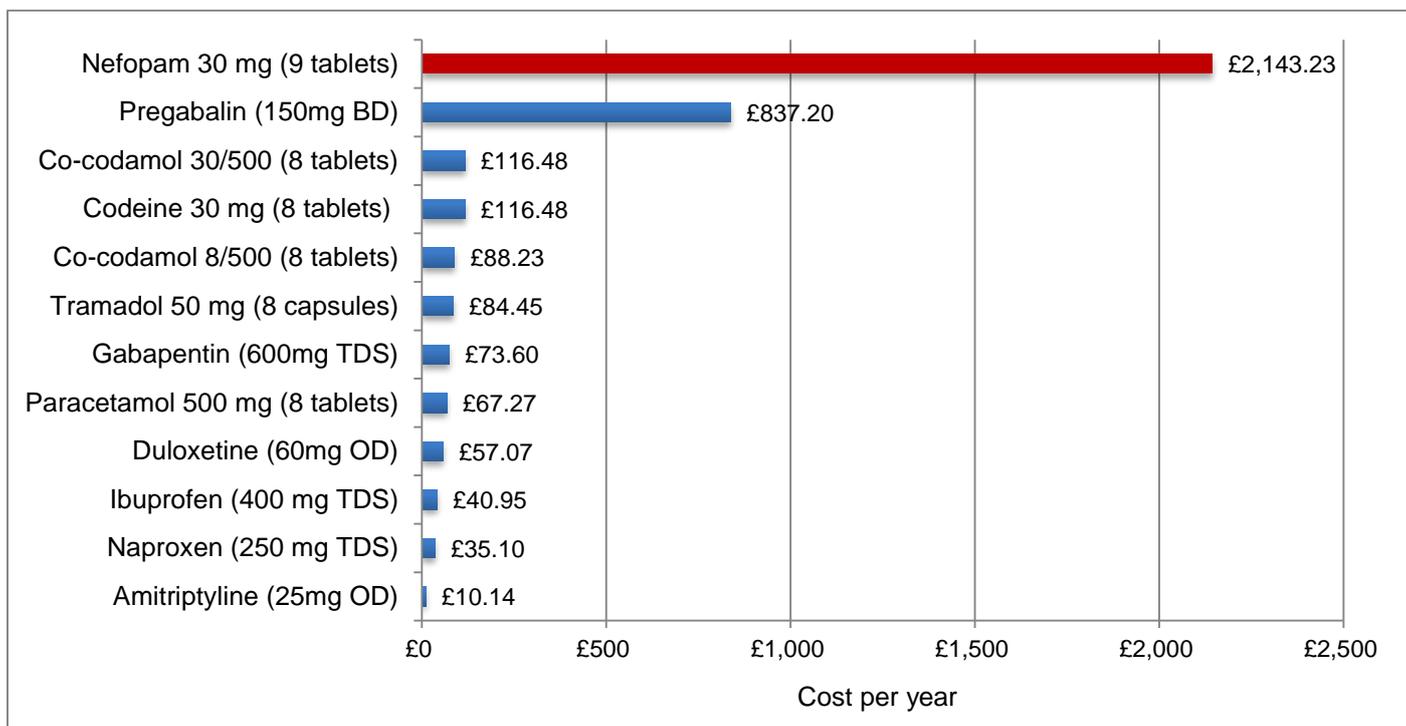
Hartlepool & Stockton-on-Tees CCG and South Tees CCG do not support the prescribing of nefopam 30mg tablets in primary care

- **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.
- Based on calculated annual treatment costs Nefopam 30mg tablets are **very expensive**, see cost comparison chart Appendix 1
- Nefopam is **not generally recommended**, and should only be considered **5th line** to manage central nociceptive pain after amitriptyline, gabapentin, duloxetine or pregabalin have proven to be either ineffective not tolerated. In such extreme cases nefopam should be initially trialled for no more than 2 weeks, reviewed regularly and discontinued if ineffective, or if unacceptable adverse effects develop.
- 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 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** through its psychostimulant-like effects linked to its dopamine reuptake inhibition properties⁷ and its anticholinergic action as a deliriant. There are reports nefopam is being increasingly identified on drug screening results.
- 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,⁸ see Appendix 2 for suggested withdrawal protocol if considered necessary.

NB: Hartlepool & Stockton-on-Tees CCG are currently consulting with North Tees & Hartlepool Foundation Trust on the continued need for nefopam in the Formulary with a view to its removal.

- **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
 - **only continue** nefopam in line with the recommendations of the specialist pain service
 - **review existing patients** – assess benefits versus adverse effects and consider stopping; withdraw slowly over 1-2 weeks following chronic use

Appendix 1 Cost comparison chart (based on July 2016 prices)



Appendix 2 Suggested slow and gradual treatment withdrawal

Adult: Initially 60mg 3 times a day, adjusted according to response; usual dose 30-90mg 3 times a day

Elderly: Initially 30mg 3 times a day, adjusted according to response; usual dose 30-90mg 3 times a day

Suggested dose reduction based on number of 30mg tablets:

Daily dose 90mg TDS

Dose timing	Chronic dose	1 st week reduction	2 nd week reduction	3 rd week
Morning	3	2	1	Stop and review Consider need to withdraw more slowly over a further 2 weeks based on withdrawal symptoms
Afternoon	3	2	1	
Evening	3	2	1	

Daily dose 30mg TDS

Dose timing	Chronic dose	1 st week reduction	2 nd week reduction	3 rd week
Morning	1	1	0	Stop and review
Afternoon	1	0	0	
Evening	1	1	1	

References

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5. M. S. Evans; C. Lysakowski; M. R. Tramèr. Nefopam for the Prevention of Postoperative Pain: Quantitative Systematic Review Br J Anaesth. 2008; 101(5):610-617.
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