Barnsley APC Position Statement on Nefopam

Barnsley APC does not support the prescribing of nefopam 30mg tablets in primary care.

- **Nefopam** is a non-opioid analgesic considered to act centrally, with associated antimuscarinic and sympathomimetic effects. [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. Patients should be counselled to advise that some level of pain is to be expected and the use of drugs may reduce the level of pain experienced but may not stop it altogether.
- 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 or not tolerated. It may sometimes be used as add-on therapy when pain is inadequately controlled[2]. 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**[3,4,5,6] in reducing pain in patients with RA or postoperative period.
- **Adverse effects are common** and include nausea, sweating (1 in 13 patients[6]), dizziness, vomiting, hallucinations, confusion, urinary retention, headache, insomnia, tachycardia (1 in 7 patients[6]), palpitations convulsions and anaphylaxis
- Nefopam scores 2 on the **anticholinergic burden** scale (ACB).[7] 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 properties[8] and its anticholinergic action as a deliriant. There are reports nefopam is being increasingly identified on drug screening results.
- Based on calculated annual treatment costs Nefopam 30mg tablets are also **relatively expensive,** see cost comparison chart Appendix 1.
- 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[9] see Appendix 2 for suggested withdrawal protocol if considered necessary.

- **Bottom line :** what does this mean in practice?

  - **do not initiate** nefopam for acute or chronic pain
  - **do not continue** nefopam routinely post discharge following secondary care acute initiation.
  - Nefopam can be used as an option in Secondary care in order to control pain in the acute phase. A 5 day supply will be given and then patients will be changed to an alternative. If patients are discharged within five days then the GP should not continue nefopam but change to an alternative.
  - nefopam should usually only be continued in line with the recommendations from the specialist pain clinic
  - **review existing patients on a case by case basis –** assess benefits versus adverse effects and consider stopping after discussion with patient; withdraw slowly over 1-2 weeks following chronic use

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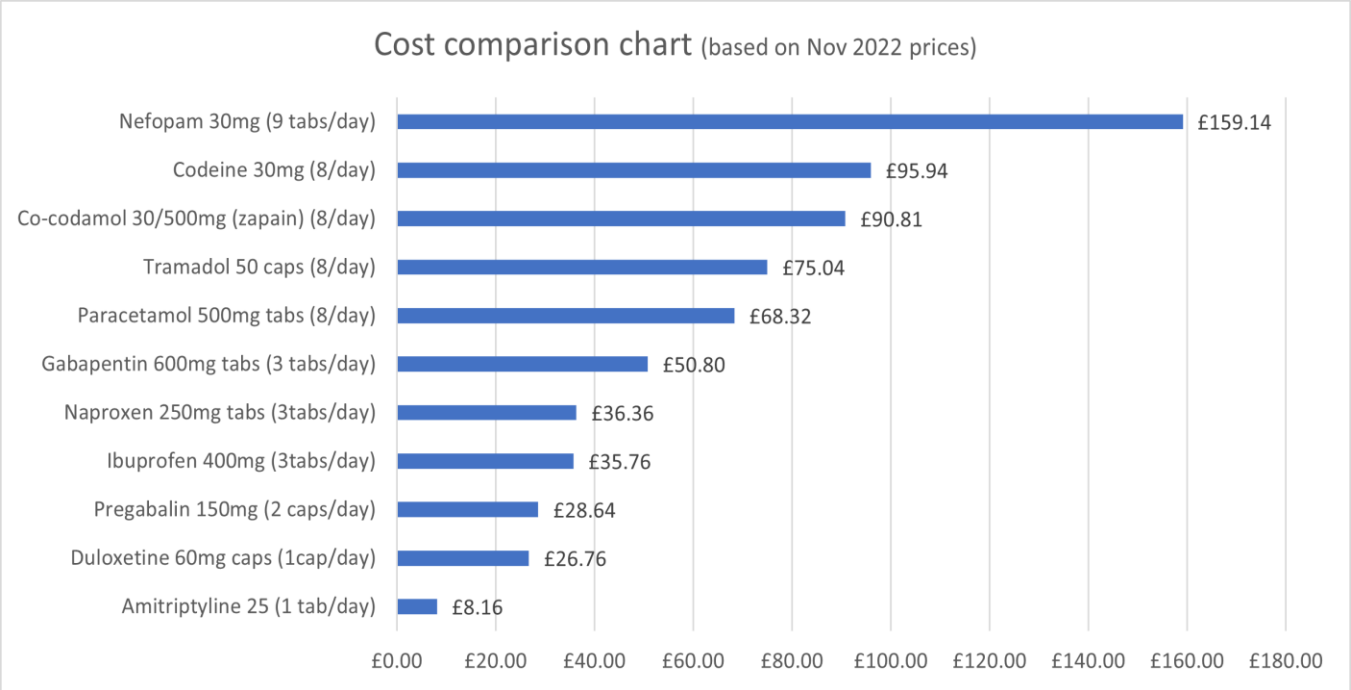
Appendix 1 Cost comparison chart (based on November 2022[10] prices)



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**	**1st week reduction**	**2nd week reduction**	**3rd 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**	**1st week reduction**	**2nd week reduction**	**3rd week**
Morning	1	1	0	Stop and review
Afternoon	1	0	0	
Evening	1	1	1	

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