NHS

County Durham & Tees Valley
Area Prescribing Committee

County Durham & Tees Valley APC Position Statement on Nefopam

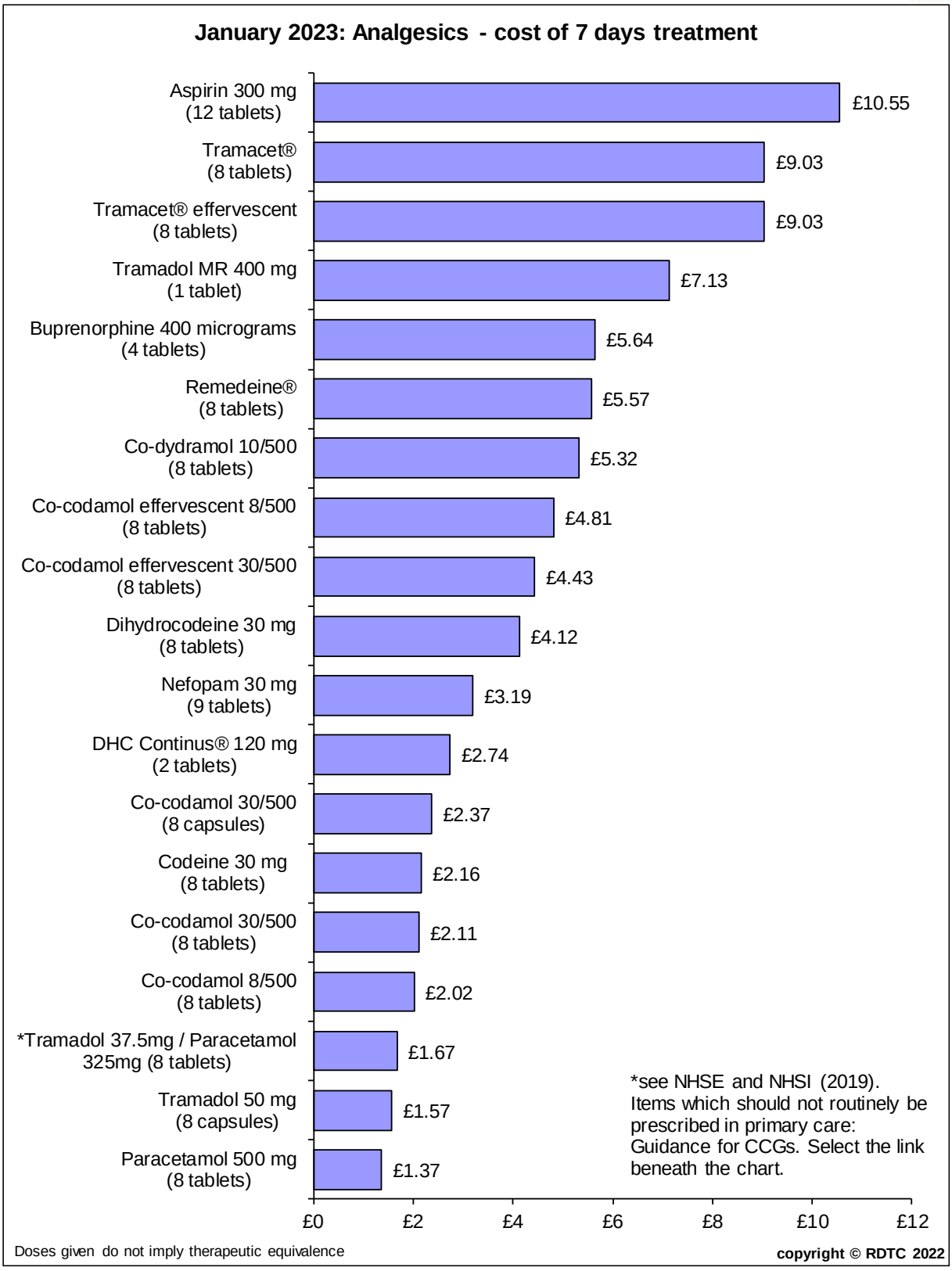
County Durham & Tees Valley APC do not support the prescribing of nefopam 30mg tablets in primary care unless on the recommendation of specialist pain services.

- 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 nonopioid 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.
- Nefopam should not be prescribed in primary care unless on the recommendation of specialist pain. It 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 properties[7] 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.

Bottom line what does this mean in practice?

- **don't initiate** nefopam for acute or chronic pain in primary care
- **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



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	

References

1. RDTC SAFER MEDICATION USE Nefopam No 14 January 2015
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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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8. Patricia A. Marken, Steven C. Stoner, Mark T. Anticholinergic Drug Abuse and Misuse Epidemiology and Therapeutic Implications Bunker Review Articles Adverse Effects CNS Drugs March 1996, Volume 5, Issue 3, pp 190-199
9. Hartlepool & Stockton-on-Tees CCG and South Tees CCG Position Statement on Nefopam September 2016