DERBYSHIRE JOINT AREA PRESCRIBING COMMITTEE (JAPC)

Nefopam

Background

JAPC makes its decision for formulary inclusion based on clinical effectiveness, safety, patient factors and cost effectiveness. In November 2016 JAPC classified nefopam as **Do Not Prescribe (DNP)** (not recommended or commissioned) due to a lack of data on effectiveness, safety concerns, and it not being cost-effective compared with standard therapy.

For a period of 12 months from July 2015 to June 2016, the four CCGs of Derbyshire dispensed approximately 38,000 items at a cost of almost £1.4 million. This was despite the fact that nefopam already had a limited place in local guidance (GREY – October 2013) as a 3rd line option in patents with contraindications or intolerance to NSAIDs or opiates. Since then the medicines management team have worked to support prescribers in reviewing patients on chronic treatment. Derbyshire prescribing for the same 12 months period (June 2017 – July 2018) has reduced to approximately 12,500 items at a cost of £360,000.

What does the literature say?

BNF: Nefopam hydrochloride may have a place in the relief of persistent pain unresponsive to other non-opioid analgesics. It causes little or no respiratory depression, but sympathomimetic and antimuscarinic side-effects may be troublesome

SPC: Nefopam is indicated for the relief of acute and chronic pain, including post-operative pain, dental pain, musculo-skeletal pain, acute traumatic pain and cancer pain
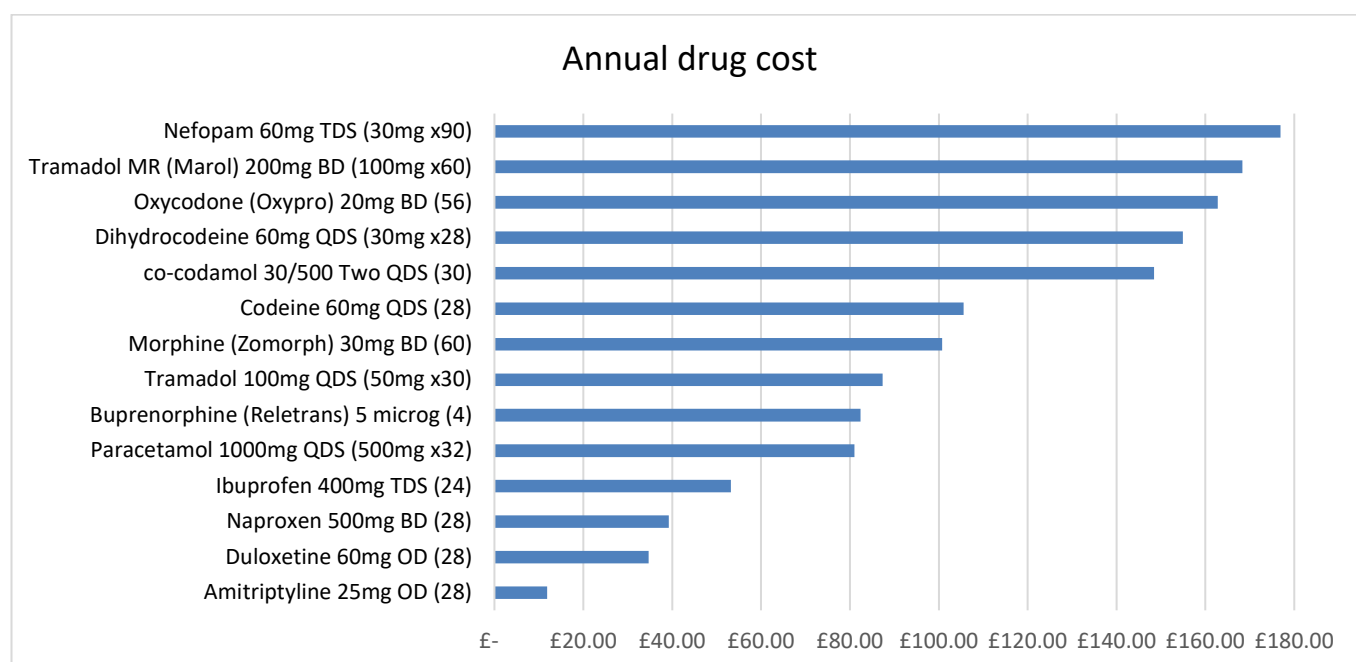
A literature review undertaken by knowledge services searching NICE, SIGN, TRIP, Cochrane Library, Scottish Medicines consortium, UKMI, Wales Medicines strategy group, Medline, EMBASE, ClinicalTrials.gov, Horizon scanning research & Intelligence. Concluded that the evidence for nefopam is weak and derived from short term studies and its place in national or nationally recognised guidelines absent. There is no mention in guidelines from the USA, Canada, Australia/New Zealand. In summary:

➤ For chronic pain the Scottish Intercollegiate Guidelines Network (SIGN) stated that 'The evidence identified on the use of nefopam for chronic pain relief is not sufficient to support a recommendation'.

➤ In inflammatory arthritis a Cochrane systematic review concluded 'based on 3 small trials, which were all at high risk of bias, there is weak evidence that nefopam and capsaicin are superior to placebo in reducing pain in patients with RA, but both are associated with a significant side effect profile'

➤ A Cochrane review looked at single dose oral nefopam for acute postoperative pain in adults. With the authors concluding 'In the absence of evidence of efficacy for oral nefopam in acute postoperative pain, its use in this indication is not justified. Because trials clearly demonstrating analgesic efficacy in the most basic of acute pain studies are lacking, use in other indications should be evaluated carefully…'

There is some evidence of the effectiveness of nefopam in peri-operative shivering where nefopam is associated with the decrease of risk of perioperative shivering following anaesthesia without influencing the extubation time when compared to placebo and clonidine.

Safety

Safety concern signals have been raised with case reports from France. Nefopam abuse causes several psychostimulant effects, such as tremor, involuntary movements, aggression, violence, agitation, facial dysaesthesia, myoclonus and sweating. Other effects include dry mouth and depression. Nefopam can contribute to anticholinergic burden.

Annual drug cost

Annual drug cost (£) bar chart:

Drug	
Nefopam 60mg TDS (30mg x90)	~£178
Tramadol MR (Marol) 200mg BD (100mg x60)	~£168
Oxycodone (Oxypro) 20mg BD (56)	~£162
Dihydrocodeine 60mg QDS (30mg x28)	~£155
co-codamol 30/500 Two QDS (30)	~£148
Codeine 60mg QDS (28)	~£106
Morphine (Zomorph) 30mg BD (60)	~£100
Tramadol 100mg QDS (50mg x30)	~£88
Buprenorphine (Reletrans) 5 microg (4)	~£82
Paracetamol 1000mg QDS (500mg x32)	~£80
Ibuprofen 400mg TDS (24)	~£53
Naproxen 500mg BD (28)	~£40
Duloxetine 60mg OD (28)	~£35
Amitriptyline 25mg OD (28)	~£13

*Above prices calculated based on drug tariff October 2021 accessed via http://www.drugtariff.nhsbsa.nhs.uk/

Stopping/switching
No protocols can be found for the switching of nefopam to either NSAIDs or alternative as listed in the costing table above. Local opinion is that for patients on long term treatment it may be advisable to taper the dose of around 30mg per day based on individual circumstances.

Conclusion
JAPC has classified nefopam as Do Not Prescribe (DNP) – not routinely recommended or commissioned. Patients already on treatment should be able to continue treatment until their next medication review where their NHS clinician might consider it appropriate to switch or stop treatment.

References
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