NHS
South West Yorkshire
Area Prescribing Committee

Medicines Safety Sub-Group

Medicines Safety Bulletin

Welcome to the first issue of the Medicines Safety Bulletin placing NEFOPAM under the spotlight.

Nefopam is a centrally acting non-opioid analgesic with associated antimuscarinic and antihistaminergic effects recommended for persistent pain unresponsive to other opioid analgesics. Prescribers need to consider carefully whether the anticipated benefits outweigh the risks of adverse effects, especially in high risk groups including the elderly.

Adverse effects are common and include nausea, sweating, dizziness, vomiting, confusion, urinary retention, headache, insomnia, tachycardia, palpitations, convulsions and anaphylaxis. Nefopam scores 2 on the **anticholinergic burden (ACB) scale.** Each one point increase in a total ACB score has been correlated with a 26% increase in the risk of death. *What other medicines with an ACB score are patients being prescribed which contribute to this increased risk?*

Drugs that have an anticholinergic burden score of 3

Chlorpromazine	Hydroxyzine
Dicycloverine	Oxybutynin
Atropine	Clemastine
Amitriptyline	Clozapine
Chlorphenamine	Glycopyrronium

Nefopam is **toxic in overdose** with observed clinical manifestations including seizures, first degree heart block, acute renal failure and heart block.
To date, 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, probably linked to its dopamine re-uptake inhibition properties.

Where nefopam has been used for its abuse potential, withdrawal may lead to depression, therefore it may be prudent to **withdraw slowly and gradually** over at least 1-2 weeks. *Refer to the sample withdrawal regimen overleaf.*

Most of the **studies** assessing the efficacy of nefopam are either single dose or short term based. The evidence base for efficacy of nefopam is **weak, conflicting or absent** in reducing pain in patients with RA or postoperative period.

Nefopam is not recommended in any national pain protocols or by national institutions associated with the management of acute, sub-acute, chronic or palliative pain. It is a relatively poorly researched drug in terms of the volume of published data and methodology.

Position Statement from Local Care Direct

"In line to support local Prescribing Guidance, Local Care Direct will advise all their prescribers not to initiate nefopam for acute or chronic pain in OOH except under advice from a specialist pain service. All repeat medication requests for nefopam will be considered on a case by case basis and if appropriate, supplies will be only be made for the duration until the patient is able to make contact with their own GP."

Example of a nefopam withdrawal regime

Suggested dose reduction based on number of 30mg tablets:

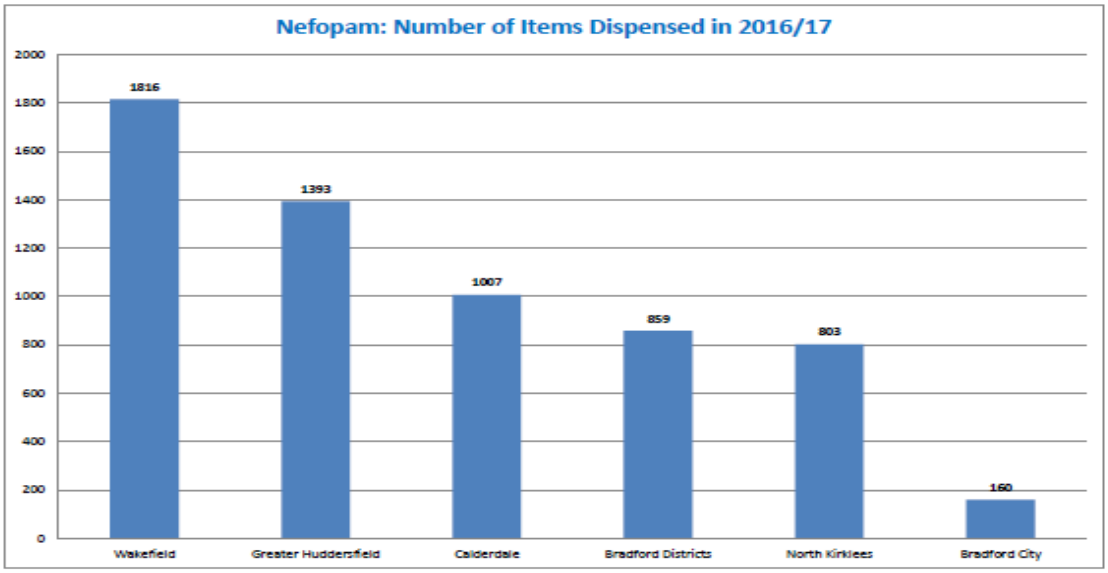
Daily dose 90mg TDS				
Dose timing	**Chronic dose**	**1st week reduction**	**2nd week reduction**	**3rd week**
Morning	3	2	1	Stop and review
Afternoon	3	2	1	Consider need to withdraw more slowly over a further 2 weeks based on withdrawal symptoms
Evening	3	2	1	

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	

Prescribing Recommendations

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. Nefopam should be initially trialled for no more than 2 weeks, reviewed regularly and discontinued if ineffective, or if unacceptable adverse effects develop.

Do not initiate or continue nefopam for acute or chronic pain except under advice from a specialist pain service.



References and Information Sources:
www.nhsbsa.nhs.uk accessed 18.10.17
www.sps.nhs.uk accessed 08.11.17 UKMI QA Nefopam
Hartlepool & Stockton-on-Tees CCG and South Tees CCG: Position Statement on Nefopam
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