Derbyshire Medicines Management UPDATE

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Pregabalin or gabapentin for neuropathic pain?

Date Updated: March 2017

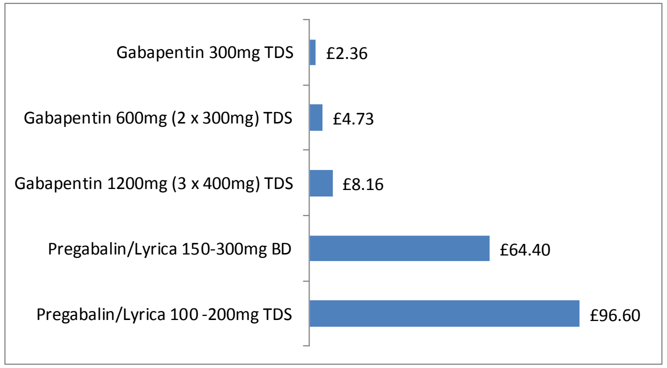
WHAT IS THE PROBLEM?

- In 2014 the NHS in the East Midlands spent nearly £17.5 million on pregabalin at an average of approximately £60 per prescription. Anecdotally, the vast majority of this prescribing was for neuropathic pain.
- If this had all been prescribed as gabapentin the equivalent cost would be £2 million; a saving of over £15 million to spend on other services.
- In 2016, Derbyshire CCGs spent **£4,051,321** on pregabalin (prescribing for all indications). If this had all been prescribed as gabapentin, the equivalent cost would be approximately **£312k**, a saving of over **£3.7million**.

WHAT IS THE EVIDENCE?

- The GABA analogues pregabalin and gabapentin are structurally and pharmacologically related. Both agents are licensed for epilepsy and peripheral neuropathic pain. Pregabalin is additionally licensed for central neuropathic pain and generalised anxiety disorders. NB: Currently, NHS England advise that the Lyrica brand of pregabalin is prescribed for the treatment of neuropathic pain (updated advice expected after July 2017).
- The NICE clinical guideline on the management of neuropathic pain[1] recommends amitriptyline (off label), duloxetine, gabapentin or pregabalin as safe and cost-effective options. NICE did not recommend one drug as clearly superior to the others and advised that the choice of treatment should be made on an individual basis.
- There are no published prospective comparative studies between pregabalin and gabapentin for post-herpetic neuralgia, diabetic neuropathy or other neuropathies apart from one small trial in neuropathic cancer pain[2]. This did not use maximal doses of both agents.
- A recent systematic review and meta-analysis concluded that tricyclic antidepressants, duloxetine, gabapentin or pregabalin could all be recommended as first-line treatments in neuropathic pain[3]. NNTs (numbers needed to treat) for 50% pain relief were **7.7** for pregabalin and **7.2** for gabapentin.
- Both gabapentin and pregabalin have propensity for misuse and Public Health England warned of this risk in 2014[4]. The document includes information on tapering and discontinuing these agents.
- Derbyshire JAPC guidance recommends amitriptyline and gabapentin as cost-effective first-line choices for neuropathic pain. The NNT for 50% pain relief is **3.6** for amitriptyline[3].

What are the costs?



Costs for 28 days supply taken from the drug tariff March 2017.
Doses are a guide and are based on licensed doses.

KEY MESSAGES

- **Pregabalin is structurally related to gabapentin and has a similar pharmacological action and adverse event profile. There are no comparative studies between pregabalin and gabapentin for post-herpetic neuralgia or diabetic neuropathy.**
- **NICE clinical guidelines recommend amitriptyline (off label), duloxetine, gabapentin or pregabalin as safe and cost-effective options for neuropathic pain. There is no evidence that one is clinically superior to another.**
- **Derbyshire JAPC guidance recommends amitriptyline and gabapentin as cost-effective first-line choices for neuropathic pain.**
- **Gabapentin needs to be given three times a day whereas pregabalin can be given twice a day. This may be of benefit to a small group of patients but will make little difference to most. Giving pregabalin three times a day is expensive so dosing should be twice a day using the lowest number of capsules.**
- **If a GABA analogue is required, gabapentin is a suitable first-line option for peripheral neuropathic pain in preference to pregabalin.**

References:

1. NICE Clinical Guideline 173 2013 Neuropathic pain: The pharmacological management of neuropathic pain in adults in non-specialist settings Available from www.nice.org.uk
2. Mishra S, Bhatnagar S, Goyal GN et al A Comparative Efficacy of Amitriptyline, Gabapentin, and Pregabalin in Neuropathic Cancer Pain: A Prospective Randomized Double-Blind Placebo-Controlled Study Am J Hosp Pall Med 2012; 29(3) 177-182
3. Finnerup NB et al. Pharmacotherapy for neuropathic pain in adults: A systematic review and meta-analysis. Lancet Neurology 2015; 14: 162-173
4. Public Health England. Advice for prescribers on the risk of the misuse of pregabalin and gabapentin. December 2014. Available from www.evidence.nhs.uk

Pregabalin or Gabapentin for Neuropathic Pain?

Date Updated: March 2017

Summary of results from Finnerup et al. meta-analysis (from www.practiceupdate.com accessed 5/10/15)

This is a systematic review and meta-analysis of 229 studies that updates the recommended pharmaceutical therapies for treating neuropathic pain. The first-line drugs are summarized in the table below.
Updates from this review include adding extended-release gabapentin enacarbil and duloxetine to first-line treatment and sending lidocaine patches and opioids down the list due to poor evidence of benefit (lidocaine) and high risk for harm (opioids). Although lidocaine and capsaicin patches are second-line treatments, they are still a good choice for those who cannot tolerate oral medicines (elderly) due to safety. Rounding out the second-line recommendations are tramadol and subcutaneous botulinum toxin A.
Few of these 229 studies lasted longer than 12 weeks and thus tolerance to therapy could not be evaluated. The NNT of 7.2 for gabapentin was calculated from studies including both immediate release (NNT = 6.3) and extended-release (NNT = 8.3) gabapentin.

First Line Pharmaceuticals for Neuropathic Pain

Drug	Dose	NNT/NNH	Cost
Gabapentin	1200-3600 mg in 3 divided doses	6.3/25.6	$
Gabapentin Enacarbil *(Extended Release)*	1200-3600 mg in 2 divided doses	8.3/31.9	$$
Pregabalin	300-600 mg in 2 divided doses	7.7/13.9	$$
Serotonin-Noradrenaline Reuptake Inhibitor	Duloxetine 60-120, once daily Venlafaxine 150-225 mg, once daily	6.4/11.8	$$
Tricyclic *(Amitriptyline)*	25-150 mg, once daily or 2 divided doses	3.6/13.4	$

NNT=Number Needed to Treat (Low # best), NNH=Number Needed to Harm (High # best)

The trial in neuropathic cancer pain[2] was a 4-week prospective randomised trial conducted in India which enrolled 120 patients with severe neuropathic cancer pain. Patients were randomised to amitriptyline 50mg daily increasing weekly to 100mg daily by week 3, gabapentin 300mg tds increasing to 600mg tds by week 3, pregabalin 75mg bd increasing to 300mg bd by week 3 or placebo. Thus patients were titrated to the maximal licensed dose of pregabalin but a sub-maximal dose of gabapentin. The primary outcome measure was efficacy as measured on a 100mm visual analogue scale (VAS, 0mm no pain, 100mm unbearable pain). However baseline VAS scores were 7.47-7.77, suggesting a 10-point scale was used. In addition, oral morphine was given for rescue analgesia at any time if the VAS was >3, again suggesting a 10 point scale and potentially affecting the resultant pain scores. The mean VAS score reductions from baseline to week 4 were 7.77 to 3.23 for amitriptyline; 7.5 to 3.07 for gabapentin; 7.77 to 2.5 for pregabalin and 7.47 to 3.4 for placebo. There is no mention of whether all patients completed the study. Given the issues with trial design and inconsistencies in presentation of results, this trial cannot be relied upon.

Cost Comparisons

The quoted cost comparison is made using the average cost per item – Pregabalin average cost per item = £63.57, gabapentin = £4.91. So, gabapentin costs about 0.077 times as much as pregabalin leading to a cost of about £287,166 if all pregabalin was prescribed as gabapentin.