

Pregabalin or gabapentin for neuropathic pain?

The NICE guidelines on neuropathic pain (1,2) recommend amitriptyline or pregabalin first line (1). They say that if satisfactory pain reduction is obtained with amitriptyline but the person cannot tolerate the adverse effects, consider oral imipramine or nortriptyline as an alternative (1) (NB the use of tricyclics for this indication is unlicensed).

However gabapentin is also licensed for the treatment of neuropathic pain but costs a fraction of pregabalin. So why don't NICE recommend gabapentin?

The NICE guideline development group agreed that there is evidence for the efficacy of pregabalin and gabapentin for the treatment of neuropathic pain. They give the following reasons for choosing pregabalin over gabapentin:

- Evidence from indirect comparisons of meta-analyses of the two treatments showed that pregabalin has lower NNT values for at least 30% pain reduction and at least 50% pain reduction compared with gabapentin, with a similar adverse-effect profile.
- Pregabalin has simple dosing and titration compared with gabapentin.
- Cost-effectiveness modelling showed that pregabalin is more cost effective than gabapentin.

It should be noted that **both gabapentin and pregabalin are highly effective in reducing pain in peripheral neuropathy.**

In a report of one systematic review the Scottish Medicines Consortium reported Pregabalin 150mg to 600mg had an NNT of 4.2 and Gabapentin (at all doses) had an NNT of 5.1 (3) to produce a 50% reduction in pain score.

The decision by NICE has been criticised. The Drug and Therapeutics Bulletin (DTB) questions the recommendation in the recent guideline and noted that pregabalin is still a black triangle drug and this too should be considered in any comparison with the much longer established gabapentin.(4) The DTB concludes: "the guideline's promotion of pregabalin creates a dilemma for those who know from the published data that gabapentin remains an effective treatment option for neuropathic pain. Gabapentin is by far the cheaper of the two drugs and therefore for the same level of investment, the NHS faces the choice of treating more patients with a cheaper but (on indirect evidence) slightly less effective drug, or fewer patients with a more expensive, seemingly more effective one. So can clinicians be sure that a

wholesale switch away from using gabapentin is a justifiable and affordable investment option? At a time of belt-tightening in the NHS, this could be a particularly expensive capsule to swallow."

The Scottish Medicines Consortium (3) concluded that pregabalin is restricted to use in patients who have not achieved adequate pain relief from or have not tolerated, conventional first and second line treatments for peripheral neuropathic pain. Treatment should be stopped if the patient has not shown sufficient benefit within 8 weeks of reaching the maximally tolerated therapeutic dose.

If you do decide to use gabapentin the following may be helpful:

Licenses

Pregabalin -neuropathic pain: pregabalin treatment can be started at a dose of 150 mg per day given as two or three divided doses. Based on individual patient response and tolerability, the dose may be increased to 300 mg per day after an interval of 3 to 7 days, and if needed, to a maximum dose of 600 mg per day after an additional 7-day interval.(5)

Gabapentin - the treatment of peripheral neuropathic pain such as painful diabetic neuropathy and post-herpetic neuralgia in adults.(6)

Neuropathic pain: Adults over 18 years. 300mg once daily on day 1, then 300mg twice daily on day 2, then 300mg 3 times a day on day 3, or initially 300mg 3 times a day, then increased according to response in steps of 300mg daily (in 3 divided doses) every 2-3 days to maximum of 3.6 grams daily.(7)

NB dose reductions are necessary for both drugs in renal impairment (see next page)

Acquisition cost examples

Drug	Dose	Cost/month	Cost/year
Pregabalin 75mg	1 twice daily	£64.40	£772.80
Pregabalin 150mg	1 twice daily	£64.40	£772.80
Pregabalin 300mg	1 twice daily	£64.40	£772.80
Gabapentin 300mg	1 three times a day	£7.42	£89.04
Gabapentin 300mg	2 three times a day	£14.83	£177.96
Gabapentin 300mg	3 three times a day	£22.25	£267.00

NB 300mg gabapentin capsules are better value for money than 600mg

"dose optimising" pregabalin will save money i.e. giving 2 x 75mg rather than 1x 150mg costs twice as much

There are no head to head studies or dose equivalence studies.



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Dosage adjustment in renal impairment

Pregabalin dose adjustment based on renal function (4)

Creatinine clearance (CL _{cr}) (mL/min)	Total pregabalin daily dose *		Dose regimen
	Starting dose (mg/day)	Maximum dose (mg/day)	
≥ 60	150	600	BID or TID
≥ 30 - <60	75	300	BID or TID
≥ 15 - <30	25 – 50	150	Once Daily or BID
< 15	25	75	Once Daily
Supplementary dosage following haemodialysis (mg)			
	25	100	Single dose ⁺

TID = Three divided doses , BID = Two divided doses

* Total daily dose (mg/day) should be divided as indicated by dose regimen to provide mg/dose

⁺ Supplementary dose is a single additional dose

Gabapentin dose adjustment based on renal function (5)

Creatinine Clearance (ml/min)	Total Daily Dose ^a (mg/day)
≥ 80	900-3600
50-79	600-1800
30-49	300-900
15-29	150 ^b -600
<15 ^c	150 ^b -300

a Total daily dose should be administered as three divided doses. Reduced dosages are for patients with renal impairment (creatinine clearance < 79 ml/min).

b To be administered as 300 mg every other day.

c For patients with creatinine clearance <15 ml/min, the daily dose should be reduced in proportion to creatinine clearance (e.g., patients with a creatinine clearance of 7.5 ml/min should receive one-half the daily dose that patients with a creatinine clearance of 15 ml/min receive).

References.

1. NICE March 2010: CG96 Neuropathic pain - pharmacological management: quick reference guide
2. Neuropathic pain. The pharmacological management of neuropathic pain in adults in non specialist settings. Guideline number 96. March 2010.
3. http://www.scottishmedicines.org.uk/files/pregabalin_Lyrica_2nd_Resubmission_FINAL_April_2009_for_website.pdf
4. Why pregabalin? Drugs and Therapeutics Bulletin. 2010;48;61
5. <http://www.medicines.org.uk/EMC/medicine/14651/SPC/Lyrica+Capsules/>
6. <http://www.medicines.org.uk/EMC/medicine/17095/SPC/Neurontin+Capsules+and+Tablets/>
7. BNF (March 2010) Section 4.8.1 page 277.

