

GABAPENTIN

CLINICAL QUESTION

Is gabapentin (GBP) safe and effective in the management of non-malignant chronic pain \geq 3 months' duration?

THE EVIDENCE

Treatment	Condition	Comparator	Relevant Results/Authors' Conclusions [#]
REVIEW ONE [†] Gabapentin (GBP) up to 3600 mg/day for 8 weeks	Post-herpetic neuralgia (PHN) and painful diabetic neuropathy (PDN)	Placebo	Moderate evidence that patients improved on GBP but that GBP is not superior to carbamazepine ^a (200 mg to 600 mg/day for 2 weeks) or phenytoin ^a (300 mg/day for 2 weeks).
REVIEW TWO [‡] Antidepressants (tricyclic and selective serotonin reuptake inhibitors) and anticonvulsants	PHN and PDN	Placebo	Strong to moderate evidence that antidepressants and anticonvulsants (GBP up to 3600 mg/day, carbamazepine ^a up to 600 mg/day, phenytoin ^a 300 mg/day) are equally effective, compared to placebo, and have the same incidence of minor adverse effects. There were fewer study withdrawals following treatment with anticonvulsants, compared with antidepressants, but the magnitude of this difference was small. No evidence that GBP is better than older anticonvulsants.
REVIEW THREE [§] GBP (varying dosages and duration of treatment)	Neuropathic pain syndromes including PHN and PDN	Placebo and other drugs	Moderate evidence that GBP is effective for several different neuropathic conditions, but effectiveness may be reduced when low doses of GBP are used. Moderate evidence that GBP (up 1800 mg/day for 6 weeks) and amitriptyline ^a (up to 75 mg/day for 6 weeks) are equally effective in treating PDN. Unable to determine if GBP is safer, when compared to amitriptyline ^a , for patients with PDN.

[†] Based on two **GOOD*** quality randomized controlled trials (RCTs) (one on PDN and one on PHN), as assessed by the authors of this review, published in 1966 and 1999; [‡]Based on five **GOOD*** quality RCTs for anticonvulsants (four on PDN and one on PHN) and 19 RCTs for antidepressants published between 1950 and 1999; [§]Based on 30 uncontrolled studies and six **AVERAGE*** quality RCTs (one on PHN and three on PDN - comparator placebo; two on PDN - comparator amitriptyline); [#]Refer to Grading Key document for explanation of evidence grading

ADDITIONAL NOTES

In Canada, GBP (Neurotin[®]) is available as an anticonvulsant and has a Notice of Compliance only for the management of patients with epilepsy who have failed to control their seizures with conventional therapy.

In the USA, GBP (Neurotin[®]) is approved by the Food and Drug Administration as an adjunct therapy for partial epilepsy and the management of post-herpetic neuralgia.

^aDrugs included in the Compendium of Pharmaceuticals and Specialties (2004): carbamazepine (Tegretol[®]), phenytoin (Dilantin), and amitriptyline (Apo[®]-Amitriptyline).

Guidelines from the Washington State Department of Labor and Industries and the Washington State Medical Association state that Neurontin[®] (GBP) is most likely effective for neuropathic pain conditions, but not for non-neuropathic pain. Similarly, the guideline from an Expert Panel on Mechanisms and Treatment of Neuropathic Pain recommends GBP as a treatment option for neuropathic pain in certain clinical circumstances.

IMPLICATIONS FOR PRACTICE

What we don't know:

- Is GBP effective for conditions other than post-herpetic neuralgia and painful diabetic neuropathy?
- What is the most effective dose of GBP (studies report doses of between 300 mg and 3600 mg per day)?
- What is the long-term effectiveness (> 3 months), safety, and tolerability of GBP?
- Are the therapeutic effects, tolerability, and safety of GBP better than those of older generation anticonvulsants and antidepressants?

Research Evidence: What we know

In patients with post-herpetic neuralgia or painful diabetic neuropathy, the evidence indicates that gabapentin:

- is more effective than placebo;
- provides significant pain relief with minimal adverse effects;
- improves measures of sleep, mood, and quality of life, as well as patient and clinician-based assessments of change;
- is safe and well tolerated in the short term.

The most commonly observed **side effects** reported are somnolence, dizziness, sedation, fatigue, and ataxia. Gabapentin may be an alternative for patients when traditional agents are contraindicated.

Gabapentin and antidepressants are both effective in the treatment of post-herpetic neuralgia and painful diabetic neuropathy and have a similar adverse effect burden.

Recommendation from Clinical Ambassadors

Gabapentin is an appropriate first line drug for neuropathic pain.

The effective daily dose varies widely (100 mg to 6000 mg) and is impossible to predict from patient to patient.

Adverse effects can be decreased and tolerability increased by initiating gabapentin at a very low dose and increasing very gradually.

The Clinical Ambassadors: Dr Pamela Barton, Dr Saifee Rashid, Dr Paul Taenzer

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Reference: This Evidence Brief is based on results from three systematic reviews (SRs) that **were not assessed** for their methodological quality. Corabian P. *Gabapentin for non-malignant chronic pain*. Edmonton, Alberta: Alberta Heritage Foundation for Medical Research, Health Technology Assessment; 2004 Jul. Report: TechNote 47. Available upon request: info@ihe.ca.

***Quality ratings for RCTs:** Good ● Average ● Poor ●

[Key to Evidence Gradings](#)

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