Medicine by the Numbers

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The NNT Group rating system:

Green:	Benefits greater than harms
Yellow:	Unclear benefits
Red:	No benefits
Black:	Harms greater than benefits

Gabapentin for Chronic Neuropathic Pain

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GABAPENTIN (NEURONTIN) FOR CHRONIC NEUROPATHIC PAIN

Number needed to treat / number needed to harm = 8

Benefits	*Harms*
1 in 6 was helped (diabetic neuropathy)	1 in 8 was harmed (developed dizziness)
1 in 8 was helped (postherpetic neuralgia)	1 in 11 was harmed (developed somnolence)
	1 in 13 was harmed (developed ataxia)
	1 in 21 was harmed (developed edema)

Details for This Review

Study Population: Adults with postherpetic neuralgia or diabetic neuropathy

Efficacy End Points: 50% pain intensity reduction

Harm End Points: Dizziness, somnolence, ataxia, edema

Narrative: Neuropathic pain, when the pain generator is the nerve itself, occurs in a variety of conditions including diabetes mellitus and postherpetic neuropathy. The exact mechanism of action for these conditions is unclear. Some speculate that aberrant nerve signal modulation may be a culprit, which would explain why neuropathic pain rarely responds adequately to traditional analgesics, and why an effective treatment has proven elusive. Further complicating matters for patients, neuropathic pain typically is chronic in nature. Given the chronic nature and the poorly understood etiology, neuropathic pain is a challenge to treat and to study.

Patients generally consider a 50% reduction in their chronic pain a useful outcome because it has been associated with important beneficial effects on sleep interference and depression.[1] Physicians have tried a variety of medicines off-label including opiates, antidepressants, and antiepileptics to relieve patients' neuropathic pain. One such drug, gabapentin (Neurontin), received approval by the U.S. Food and Drug Administration (FDA) in 1993 as an adjunct medicine for partial seizures and additional FDA approval in 2002 for the treatment of postherpetic neuralgia.[2] Gabapentin remains off-label when used to treat diabetic neuropathy.

This summary uses a Cochrane review, updated in 2014, to address the efficacy of gabapentin compared with placebo to palliate neuropathic pain.[3] The Cochrane review includes 37 trials enrolling more than 5,600 patients. Overall, there were limited quality data to permit analysis of other neuropathic indications other than postherpetic neuralgia and diabetic neuropathy. Oral gabapentin dosed at 1,200 mg or more daily demonstrated a 50% reduction in pain intensity, with a number needed to treat (NNT) of eight for postherpetic neuralgia and an NNT of six for diabetic neuropathy. Gabapentin treatment was associated with several adverse effects including dizziness (number needed to harm [NNH] = 8), somnolence (NNH = 11), ataxia (NNH = 13), and edema (NNH = 21). There were no obvious differences in patient response with doses greater than 1,200 mg. The NNT for gabapentin is similar to a recent meta-analysis that demonstrated an NNT of seven.[4]

Caveats: The Cochrane reviewers indicated that high-quality evidence was lacking, which limits the strength of the conclusions and the resulting NNTs in this analysis. Moreover, only postherpetic neuralgia and diabetic neuropathy had been studied adequately to generate numerical estimates for the purposes

of this review. Although patients with other neuropathic conditions were included in the Cochrane review, specifically fibromyalgia, the efficacy of gabapentin could not be evaluated in the treatment of these conditions because of a lack of quality data.

The regulatory and research history of gabapentin is important and relevant in any attempt to understand how related data should be applied or extrapolated. There are a number of peer-reviewed publications,[5-7] publicly available court documents,[8] investigative lay press reports,[9] and high-profile scientific editorials[10] that all strongly suggest that available data on gabapentin cannot be comfortably extrapolated or applied to practice. For this reason, we have rated gabapentin for chronic neuropathic pain yellow, meaning we believe that a proper answer is not yet available. In the future, we hope to see high-quality, randomized, non–industry-funded data that may offer reliable and valid answers to the question of the efficacy of gabapentin for neuropathic pain and other conditions.

There are patients who appear to benefit from gabapentin. This is particularly important in the case of postherpetic neuralgia, which can severely impact quality of life, and psychological and physical well-being.[11,12] The challenge is identifying the minority of patients who derive benefit and finding the proper dose,[13] both of which seem to depend on patients' clinical response to a trial of therapy.

Notably, few guidelines exist for the treatment of neuropathic pain. One, from the National Institute for Health and Care Excellence in the United Kingdom, includes the use of gabapentin as a first-tier treatment for all neuropathic pain.[14] Similarly, the European Federation of Neurological Societies includes gabapentin as a first-tier agent in its guideline for neuropathic pain, specifically including painful polyneuropathy and postherpetic neuralgia.[15] The American Academy of Neurology with other organizations issued a joint guideline in 2011 indicating only that gabapentin should be considered for the treatment of painful diabetic neuropathy.[16]

The opinions and assertions contained herein are the private views of the author and are not to be construed as official or as reflecting the views of the U.S. Air Force medical department or the U.S. Air Force at large.

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