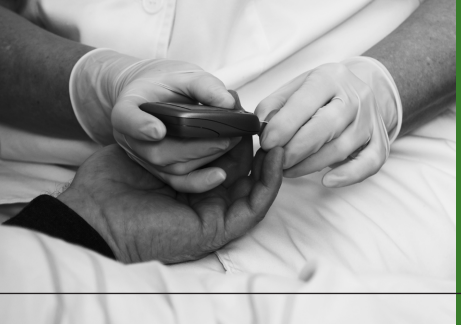

AAN Summary of Evidence-based Guideline for CLINICIANS

TREATMENT OF PAINFUL DIABETIC NEUROPATHY

This is a summary of the American Academy of Neurology (AAN) guideline update regarding pharmacologic and nonpharmacologic treatment of painful diabetic neuropathy (PDN).

Please refer to the full guideline at www.aan.com for more information, including definitions of the classifications of evidence and recommendations.

Pharmacologic Treatments

In patients with PDN, what is the efficacy of pharmacologic agents to reduce pain and improve physical function and quality of life (QOL)?

Anticonvulsants	
Strong evidence	If clinically appropriate, pregabalin should be offered for the treatment of PDN (**Level A**[+]).
Moderate evidence	Gabapentin and sodium valproate should be considered for the treatment of PDN (**Level B**).
	Oxcarbazepine, lamotrigine, and lacosamide should probably not be considered for the treatment of PDN (**Level B**).
Insufficient evidence	There is insufficient evidence to support or refute the use of topiramate for the treatment of PDN (**Level U**).
Clinical context	Although sodium valproate may be effective in treating PDN, it is potentially teratogenic and should be avoided in diabetic women of childbearing age. Due to potential adverse effects such as weight gain and potential worsening of glycemic control, this drug is unlikely to be the first treatment choice for PDN.
Antidepressants	
Moderate evidence	Amitriptyline, venlafaxine, and duloxetine should be considered for the treatment of PDN (**Level B**). Data are insufficient to recommend one of these agents over the others.
Weak evidence	Venlafaxine may be added to gabapentin for a better response (**Level C**).
Insufficient evidence	There is insufficient evidence to support or refute the use of desipramine, imipramine, fluoxetine, or the combination of nortriptyline and fluphenazine in the treatment of PDN (**Level U**).
Opioids	
Moderate evidence	Dextromethorphan, morphine sulphate, tramadol, and oxycodone should be considered for the treatment of PDN (**Level B**). Data are insufficient to recommend one agent over the other.
Clinical context	The use of opioids for chronic nonmalignant pain has gained credence over the last decade due to the studies reviewed in this article. Both tramadol and dextromethorphan were associated with substantial adverse events (e.g., sedation in 18% on tramadol and 58% on dextromethorphan, nausea in 23% on tramadol, and constipation in 21% on tramadol). The use of opioids can be associated with the development of novel pain syndromes such as rebound headache. Chronic use of opioids leads to tolerance and frequent escalation of dose.
Other Pharmacologic Agents	
Moderate evidence	Capsaicin and isosorbide dinitrate spray should be considered for the treatment of PDN (**Level B**).
	Clonidine, pentoxifylline, and mexiletine should probably not be considered for the treatment of PDN (**Level B**).
Weak evidence	The Lidoderm patch may be considered for the treatment of PDN (**Level C**).
Insufficient evidence	There is insufficient evidence to support or refute the usefulness of vitamins and α-lipoic acid in the treatment of PDN (**Level U**).
Clinical context	Although capsaicin has been effective in reducing pain in PDN clinical trials, many patients are intolerant of the side effects, mainly burning pain on contact with warm/hot water or in hot weather.

Nonpharmacologic Treatments

In patients with PDN, what is the efficacy of nonpharmacologic modalities to reduce pain and improve physical function and QOL?

Electrical Stimulation, Magnetic Field Treatment, and Other Interventions	
Moderate evidence	Percutaneous electrical nerve stimulation should be considered for the treatment of PDN (**Level B**).
	Electromagnetic field treatment, low-intensity laser treatment, and Reiki therapy should probably not be considered for the treatment of PDN (**Level B**).
Insufficient evidence	Evidence is insufficient to support or refute the use of amitriptyline plus electrotherapy for treatment of PDN (**Level U**).

Clinical Context Summary For All Evidence

It is notable that the placebo effect varied from 0% to 50% pain reduction in these studies.

Adjuvant analgesic agents are drugs primarily developed for an indication other than treatment of PDN (e.g., anticonvulsants and antidepressants) that have been found to lessen pain when given to patients with PDN. Their use in the treatment of PDN is common. The panel recognizes that PDN is a chronic disease and that there are no data on the efficacy of the chronic use of any treatment, as most trials have durations of 2 to 20 weeks. It is important to note that the evidence is limited, the degree of effectiveness can be minor, the side effects can be intolerable, the impact on improving physical function is limited, and the cost is high, particularly for novel agents.

A summary of Level A and B recommendations for the treatment of PDN is provided in the table.

Table: Summary of Recommendations

	Recommended Drug and Dose	Not Recommended
Level A	Pregabalin, 300–600 mg/day	
Level B	Gabapentin, 900–3600 mg/day Sodium valproate, 500–1200 mg/day Venlafaxine, 75–225 mg/day Duloxetine, 60–120 mg/day Amitriptyline, 25–100 mg/day Dextromethorphan, 400 mg/day Morphine sulphate, titrated to 120 mg/day Tramadol, 210 mg/day Oxycodone, mean 37 mg/day, max 120 mg/day Capsaicin, 0.075% qid Isosorbide dinitrate spray Electrical stimulation, percutaneous nerve stimulation x 3–4 weeks	Oxcarbazepine Lamotrigine Lacosamide Clonidine Pentoxifylline Mexiletine Magnetic field treatment Low-intensity laser therapy Reiki therapy

Copies of this summary and additional companion tools are available at *www.aan.com* or through AAN Member Services at (800) 879-1960.

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