

Peripheral Neuropathic Pain

Peripheral neuropathic pain (PNP) is encountered with increasing frequency in clinical practice, often in conjunction with chronic diseases such as diabetes, HIV infection, multiple sclerosis, cancer, and post-herpes simplex virus exposure.¹

The hallmark of this type of pain is allodynia or the elicitation of pain by a stimulus that is not normally considered noxious, such as light touch, pressure, or mild temperature changes.² In addition, PNP is often described as numbness, burning, tingling, or as a “pins and needles” sensation.^{1,3} It may be acute or chronic, and can remain a problem long after the precipitating event has resolved.

General Treatment Guidelines

- **The tricyclic antidepressants (TCAs) are the mainstay of PNP treatment.** A 2005 meta-analysis found that 3.5 patients had to be treated with TCAs in order for one patient to have a 50% reduction in neuropathic pain.⁴
- **Anticonvulsants have likewise been extensively studied.** The above-mentioned meta-analysis found that 2.3 to 3.8 patients treated with anticonvulsants will result in one patient with a 50% reduction in neuropathic pain.⁴ Only gabapentin (Neurontin®) and pregabalin (Lyrica®) have FDA approval for PNP.
- **Among newer antidepressants, the Serotonin Norepinephrine Reuptake Inhibitors (SNRIs) duloxetine (Cymbalta®) and venlafaxine (Effexor®) have the most data.** Duloxetine is FDA approved for diabetic neuropathy based on two randomized controlled trials.^{5,6} Venlafaxine has not been approved for this indication, but has been shown to be effective in small trials.⁷⁻⁹
- **Tramadol (Ultram®) has proven efficacy in the treatment of PNP, based on several large randomized controlled trials.** Smaller trials have compared tramadol to TCAs and morphine, but have not been conclusive.¹⁰
- **Opioid analgesics have also been shown effective, but many practitioners may be uncomfortable using them for this condition.** Recent consensus guidelines from the American Society of Pain Educators recommend that controlled-release oxycodone (OxyContin®) be considered a first-line agent, however, these guidelines are based on the number of trials available, not the quality of evidence.¹¹
- **Other agents, such as topical lidocaine, capsaicin, older anticonvulsants, and other antidepressants can be considered when treatment failure occurs.**

Treatment Option Comparison^{1,12}

Drug	Typical Daily Dose	FDA approved?	Cost*	Comments
First-Line Agents				
Amitriptyline (generic)	30-150 mg	No	\$3.99	Most anticholinergic TCA; patients may have difficulty tolerating
Desipramine (generic)	100-200 mg	No	\$37.98	Better tolerated than amitriptyline; equivalent efficacy
Nortriptyline (generic)	10-75 mg	No	\$12.99	Better tolerated than amitriptyline; equivalent efficacy
Gabapentin (generic)	300-1800 mg	Yes (post-herpetic neuralgia)	\$89.99	Better tolerated than TCAs; initiate at 100mg qhs; titrate slowly
Tramadol (generic)	150-300 mg	No	\$99.94	Dual MOA: mu-opioid agonist and inhibits reuptake of serotonin/NE
Duloxetine (Cymbalta®)	40-60 mg	Yes (diabetic neuropathy)	\$112.36	Good choice for patients with comorbid depression
Pregabalin (Lyrica®)	150-300 mg	Yes (diabetic & post-herpetic neuropathy)	\$157.97	Similar to gabapentin; however, schedule V controlled substance; Medicaid requires prior auth.
Second-Line Agents				
Venlafaxine (Effexor®)	72-225 mg	No	\$202.48	Similar MOA as duloxetine; less clinical evidence
Oxycodone ER (generic)	20-80 mg	No	~\$287.99 (pricing not available)	Opioids are generally reserved as agents of last resort or used in combination with other agents
Other Agents				
Capsaicin topical (Zostrix®)	0.025% - 0.075% cream	No	\$39.98	Must be applied 3-5 times daily for 2-4 weeks for full efficacy; tolerability often an issue
Carbamazepine (generic)	600 mg	No	\$16.65	Adverse effects and monitoring requirements limit utility
Lamotrigine (Lamictal®)	200-400 mg	No	\$272.58	Monitor for rash; Medicaid requires prior authorization

*Cost from www.drugstore.com where possible; based on high end of typical daily dose

References

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