

Comparison of Drug Therapy for National and International Neuropathic Pain Guidelines (Updated 2/8/2018)

| Guidelines | Canadian Pain Society (CPS) ¹ Updated as of Nov 2014 | Neuropathic Pain Special Interest Group (NeuPSIG/IASP) ² Updated as of Jan 2015 | National Institute for Health and Care Excellence (NICE) ³ Updated as of Feb 2017 | European Federation of Neurological Societies (EFNS) ⁴ Updated as of Apr 2010 | | |
|---------------------------------|---|---|---|---|--|---|
| Trigeminal Neuralgia | First-line: Carbamazepine | | First-line: Carbamazepine Second-line: Seek Specialist | First-line: Carbamazepine, Oxcarbazepine Second-line: Surgery | | |
| Type of Neuropathic Pain | All neuropathic pain | All neuropathic pain | All neuropathic pain | Central neuropathic pain | Diabetic neuropathy | Post-herpetic neuralgia |
| First-line | Gabapentin Pregabalin Duloxetine Venlafaxine TCAs | Gabapentin ^A Pregabalin Duloxetine Venlafaxine TCAs | Gabapentin Pregabalin Duloxetine Amitriptyline | Gabapentin Pregabalin Amitriptyline TCAs | Gabapentin Pregabalin Duloxetine Venlafaxine ER TCAs | Gabapentin Pregabalin TCAs Lidocaine plasters ^B |
| Second-line | Tramadol CR opioids: Morphine Oxycodone Fentanyl Hydromorphone | Tramadol Capsaicin 8% patches* Lidocaine patches* | If the initial treatment is not effective or is not tolerated, offer one of the remaining 3 drugs above ↑, and consider switching again if the second and third drugs tried are also not effective or not tolerated | Tramadol Opioids | Tramadol ^C | Opioids: Oxycodone Morphine Methadone Topical Capsaicin |
| Third-line | Cannabinoids | Strong Opioids: Oxycodone Morphine Botulinum toxin A* | Tramadol: acute only Topical Capsaicin* | Opioids | Opioids: Oxycodone | |
| Fourth-line /Last-line | Methadone Tapentadol Lamotrigine Topiramate Valproic Acid Citalopram Escitalopram Paroxetine Lacosamide Topical capsaicin Topical lidocaine ^D Botulinum toxin | | Specialist setting: Cannabis sativa extract Lacosamide Lamotrigine Levetiracetam Morphine Oxcarbazepine Topiramate Tramadol: long term Venlafaxine | Lamotrigine ^E Cannabinoids ^F | <p>CPSP = central post-stroke pain; CR = controlled release; ER = extended release; SCI = spinal cord injury; TCAs= tricyclic antidepressants; * For peripheral neuropathy; A = Gabapentin immediate release, extended release, and enacarbil; B = Topical lidocaine with its excellent tolerability may be considered first line in the elderly, especially if there are concerns regarding the CNS side effects of oral medications; C = Tramadol may be considered first line in patients with acute exacerbations of pain especially for the tramadol/acetaminophen combination or in patients with predominant coexisting non-neuropathic pain; D = Topical lidocaine may be second-line for postherpetic neuralgia; E = Lamotrigine may be considered in CPSP or SCI pain with incomplete cord lesion and brush-induced allodynia; F = For multiple sclerosis</p> | |

Table References

1. Moulin D, Boulanger A, Clark AJ, et al. Pharmacological management of chronic neuropathic pain: revised consensus statement from the Canadian Pain Society. *Pain Res Manag.* 2014;19:328–35.
2. Finnerup NB, Attal N, Haroutounian S, et al. Pharmacotherapy for neuropathic pain in adults: a systematic review and meta-analysis. *Lancet Neurol.* 2015;14:162–173. doi: 10.1016/S1474-4422(14)70251-0
3. National Institute for Health and Care Excellence (NICE). Neuropathic pain: the pharmacological management of neuropathic pain in adults in non-specialist settings. 2013.
4. Attal N, Cruccu G, Baron R, et al. EFNS guidelines on the pharmacological treatment of neuropathic pain: 2010 revision. *Eur J Neurol.* 2010;17:1113. doi: 10.1111/j.1468-1331.2010.02999.x

Opinion of Authors:

- We believe that if opioids are used chronically, consideration should favor opioids with pharmacological activity that aligns most closely with neuropathic pain treatment. These include tramadol, tapentadol, methadone, and levorphanol, all of which block reuptake of norepinephrine. Both methadone and levorphanol block N-methyl-D-aspartase (NMDA) receptors. Methadone and tramadol also block reuptake of serotonin. Methadone and tramadol have complex cytochrome metabolisms, both drugs of which are significantly affected by genetic polymorphisms. Levorphanol and tapentadol only undergo phase II metabolism which avoids cytochrome drug interactions and issues with genetic variability.^{1,2}
- Tramadol for as needed use is often difficult to tolerate due to serotonin activity.
- Tapentadol was approved in Europe in 2011³, EFNS guidelines were last updated in April 2010.

Opinion References

1. Zorn KE, Fudin J. Treatment of neuropathic pain: the role of unique opioid agents. *Pract Pain Manag.* 2011 May; 11 (4): 26-33.
2. Pham TC, Fudin J, Raffa RB. Is Levorphanol a Better Option Than Methadone? *Pain Med.* 2015 September; 16(9):1673-1679.
3. Palexia film coated tablets. eMC. Datapharm. Leatherhead, UK. Available at: <https://www.medicines.org.uk/emc/medicine/28375/SPC/Palexia+film+coated+tablets/>. Accessed February 7, 2018.