# Medications for Neuropathic Pain

**B.C. Provincial Academic Detailing Service** **Appendix: February 2019**

## Update 2019: Pregabalin for Neuropathic Pain

In January 2019, an update to the 2009 Cochrane systematic review of pregabalin for neuropathic pain was published.[1] The current review increases the numbers of trials and participants with neuropathic pain from 14 trials with 3680 participants to 45 trials with 11,906 participants.

## Evidence for Practice: Pregabalin for Neuropathic Pain

### Applicability

The majority of pregabalin trials enrolled participants with painful diabetic neuropathy or post herpetic neuralgia.[1]
The duration of the trials ranged from 2 to 15 weeks.[1]

### Efficacy

Cochrane systematic review of pregabalin estimates that approximately 3 to 4 people out of 10 achieve a substantial reduction in pain (50% or greater) with medication, versus 1 to 2 people receiving placebo.[1]

### Dose Response

Approximately 1 in 10 more people achieve a substantial reduction in pain with the 600 mg dose of pregabalin than the 300 mg dose.[1] Adverse events are more frequent with the higher dose.[1]

| | | | |
|---|---|---|---|
| **Pregabalin for Painful Diabetic Neuropathy** *2019 Cochrane systematic review*[1] | | | |
| Pregabalin 300 mg | | | |
| NNT 14<br>●●●●●●●●●●●●●●<br>(pregabalin: 31%; placebo: 24%) | substantial reduction in pain (50% or greater) | discontinuation due to adverse event<br>any adverse event<br>dizziness<br>somnolence | NNH 35<br>NNH 11<br>NNH 10<br>NNH 13 |
| Pregabalin 600 mg | | | |
| NNT 6<br>●●●●●●<br>(pregabalin: 42%; placebo: 25%) | substantial reduction in pain (50% or greater) | discontinuation due to adverse event<br>any adverse event<br>dizziness<br>somnolence | NNH 12<br>NNH 8<br>NNH 6<br>NNH 10 |
| **Pregabalin for Post Herpetic Neuralgia** *2019 Cochrane systematic review*[1] | | | |
| Pregabalin 300 mg | | | |
| NNT 5<br>●●●●●<br>(pregabalin: 32%; placebo: 13%) | substantial reduction in pain (50% or greater) | discontinuation due to adverse event<br>any adverse event<br>dizziness<br>somnolence | NNH 11<br>NNH 11<br>NNH 5<br>NNH 10 |
| Pregabalin 600 mg | | | |
| NNT 4<br>●●●●<br>(pregabalin: 41%; placebo: 15%) | substantial reduction in pain (50% or greater) | discontinuation due to adverse event<br>any adverse event<br>dizziness<br>somnolence | NNH 7<br>NNH 8<br>NNH 4<br>NNH 5 |

Compared to the 2009 Cochrane review, the NNTs and NNHs for painful diabetic neuropathy reflect a decrease in the estimate of the numbers of responders to pregabalin 300 mg as well as fewer people discontinuing due to adverse events. Compared to the 2009 review, NNTs and NNHs remain similar for post herpetic neuralgia. Estimates for patient's impression of change (much or very much improved) are relatively unchanged (NNTs range from 4 to 6 across doses and indications). Overall, responder rates to placebo are about 10% higher in painful diabetic neuropathy trials than in post herpetic neuralgia trials.

## Medications for Neuropathic Pain: Evidence Brief using the Cochrane Library[1-25]

| Antiepileptic Medications | | | Antidepressant Medications | | |
|---|---|---|---|---|---|
| ■ gabapentin | 37 trials | 5914 participants | ■ duloxetine | 9 trials | 2776 participants |
| ■ pregabalin | 45 trials | 11,906 participants | ■ venlafaxine | 6 trials | 460 participants |
| ■ carbamazepine | 10 trials | 480 participants | ■ amitriptyline | 17 trials | 1342 participants |
| ■ lacosamide | 5 trials | 1863 participants | ■ desipramine | 5 trials | 177 participants |
| ■ lamotrigine | 12 trials | 1511 participants | ■ nortriptyline | 6 trials | 310 participants |

**Other antiepileptic medications** ■ levetiracetam ■ oxcarbazepine ■ topiramate ■ valproic acid, divalproex sodium
**Other antidepressant medications** ■ imipramine
**Opioids** ■ hydromorphone ■ morphine ■ oxycodone ■ tramadol ■ transdermal fentanyl ■ methadone
**Other pharmacotherapies** ■ medical cannabinoids ■ acetaminophen with or without codeine ■ nonsteroidal anti-inflammatory drugs
**Combinations** ■ gabapentin or pregabalin + opioid ■ gabapentin or pregabalin + tricyclic antidepressant ■ tricyclic antidepressant + opioid

■ *high quality evidence* ➲ Cochrane reviewers are very confident that their evidence review identifies the likely therapeutic effect
■ *moderate quality evidence* ➲ Cochrane reviewers judge that their evidence review is a good indication of the likely therapeutic effect
■ *lacks clear evidence* ➲ Cochrane reviewers are not confident in the quality, quantity or consistency of the evidence for most outcomes
■ *limited or no therapeutic value* ➲ Cochrane reviewers judge that the available evidence indicates limited or no clinically relevant benefit

**Limitations of the evidence which preclude very confident conclusions about benefits and harms:**[1-25]

- trials were few in number or small in size (eg, fewer than 200 participants per treatment arm)
- short trial durations limit satisfactory assessment of efficacy and safety
- data on specific benefits (eg, numbers of people with a substantial reduction in pain) or harms (eg, serious adverse events) were not available from all trials
- incomplete accounting for participants' outcomes after they withdrew from the trial or discontinued treatment
- methods of blinding participants and personnel to treatment assignments were inadequately implemented or described
- manufacturer sponsorship of all or most of the identified trials

Carbamazepine Health Canada pain indication: symptomatic relief of pain of trigeminal neuralgia during exacerbation[26]

## REFERENCES


1. Derry S, Bell R, Straube S, et al. Pregabalin for neuropathic pain in adults. Cochrane Database of Systematic Reviews 2019, Issue 1. Art. No. CD007076
2. Wiffen P, Derry S, Bell R, et al. Gabapentin for chronic neuropathic pain in adults. Cochrane Database of Systematic Reviews 2017, Issue 6. Art. No. CD0007938
3. Wiffen P, Derry S, Moore R, et al. Carbamazepine for chronic neuropathic pain and fibromyalgia in adults. Cochrane Database of Systematic Reviews 2014, Issue 4. Art. No. CD005451
4. Hearn L, Derry S, Moore R. Lacosamide for neuropathic pain and fibromyalgia in adults. Cochrane Database of Systematic Reviews 2012, Issue 2. Art. No. CD009318
5. Wiffen P, Derry S, Moore R. Lamotrigine for chronic neuropathic pain and fibromyalgia in adults. Cochrane Database of Systematic Reviews 2013, Issue 12. Art. No. CD006044
6. Lunn M, Hughes R, Wiffen P. Duloxetine for treating painful neuropathy, chronic pain or fibromyalgia. Cochrane Database of Systematic Reviews 2014, Issue 1. Art. No. CD007115
7. Gallagher H, Gallagher R, Butler M, et al. Venlafaxine for neuropathic pain in adults. Cochrane Database of Systematic Reviews 2015, Issue 8. Art. No. CD011091
8. Moore R, Derry S, Aldington D, et al. Amitriptyline for neuropathic pain in adults. Cochrane Database of Systematic Reviews 2015, Issue 7. Art. No. CD008242
9. Hearne L, Moore R, Derry S, et al. Desipramine for neuropathic pain in adults. Cochrane Database of Systematic Reviews 2014, Issue 9. Art. No. CD011003
10. Derry S, Wiffen P, Aldington D, et al. Nortriptyline for neuropathic pain in adults. Cochrane Database of Systematic Reviews 2015, Issue 1. Art. No. CD011209
11. Wiffen P, Derry S, Moore R, et al. Levetiracetam for neuropathic pain in adults. Cochrane Database of Systematic Reviews 2017, Issue 5. Art. No. CD012499
12. Zhou M, Chen N, He L, et al. Oxcarbazepine for neuropathic pain. Cochrane Database of Systematic Reviews 2017, Issue 12. Art. No. CD007963
13. Wiffen P, Derry S, Lunn M, et al. Topiramate for neuropathic pain and fibromyalgia in adults. Cochrane Database of Systematic Reviews 2013, Issue 8. Art. No. CD008314
14. Gill D, Derry S, Wiffen P, et al. Valproic acid and sodium valproate for neuropathic pain and fibromyalgia in adults. Cochrane Database of Systematic Reviews 2011, Issue 10. Art. No. CD009183
15. Hearn L, Derry S, Phillips T, et al. Imipramine for neuropathic pain in adults. Cochrane Database of Systematic Reviews 2014, Issue 5. Art. No. CD010769
16. Stannard C, Gaskell H, Derry S, et al. Hydromorphone for neuropathic pain in adults. Cochrane Database of Systematic Reviews 2016, Issue 5. Art. No. CD011604
17. Cooper T, Chen J, Wiffen P, et al. Morphine for chronic neuropathic pain in adults. Cochrane Database of Systematic Reviews 2017, Issue 5. Art. No. CD011669
18. Gaskell H, Derry S, Stannard C, et al. Oxycodone for neuropathic pain in adults. Cochrane Database of Systematic Reviews 2016, Issue 7. Art. No. CD010692
19. Duehmke R, Derry S, Wiffen P, et al. Tramadol for neuropathic pain in adults. Cochrane Database of Systematic Reviews 2017, Issue 6. Art. No. CD003726
20. Derry S, Stannard C, Cole P, et al. Fentanyl for neuropathic pain in adults. Cochrane Database of Systematic Reviews 2016, Issue 10. Art. No. CD011605
21. McNicol E, Ferguson M, Schumann R. Methadone for neuropathic pain in adults. Cochrane Database of Systematic Reviews 2014, Issue 7. Art. No. CD010943
22. Mucke M, Phillips T, Radbruch L, et al. Cannabis-based medicines for chronic neuropathic pain in adults. Cochrane Database of Systematic Reviews 2018, Issue 3. Art. No. CD012182
23. Wiffen P, Knaggs R, Derry S, et al. Paracetamol (acetaminophen) with or without codeine or dihydrocodeine for neuropathic pain in adults. Cochrane Database of Systematic Reviews 2016, Issue 12. Art. No. CD012227
24. Moore R, Chi C, Wiffen P, et al. Oral nonsteroidal anti-inflammatory drugs for neuropathic pain. Cochrane Database of Systematic Reviews 2015, Issue 10. Art. No. CD010902
25. Chapparro L, Wiffen P, Moore R, et al. Combination pharmacotherapy for the treatment of neuropathic pain in adults. Cochrane Database of Systematic Reviews 2012, Issue 7. Art. No. CD008943
26. Health Canada Product Monograph. Tegretol (carbamazepine). [Internet]. http://webprod5.hc-sc.gc.ca/dpd-bdpp/