Update 2019: Pregabalin for Neuropathic Pain

In January 2019, an update to the 2009 Cochrane systematic review of pregabalin for neuropathic pain was published. 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

<table>
<thead>
<tr>
<th>Applicability</th>
<th>Efficacy</th>
<th>Dose Response</th>
</tr>
</thead>
<tbody>
<tr>
<td>The majority of pregabalin trials enrolled participants with painful diabetic neuropathy or post herpetic neuralgia. The duration of the trials ranged from 2 to 15 weeks.</td>
<td>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.</td>
<td>Approximately 1 in 10 more people achieve a substantial reduction in pain with the 600 mg dose of pregabalin than the 300 mg dose. Adverse events are more frequent with the higher dose.</td>
</tr>
</tbody>
</table>

#### Pregabalin for Painful Diabetic Neuropathy 2019 Cochrane systematic review

<table>
<thead>
<tr>
<th>Dose</th>
<th>NNT</th>
<th>NNH</th>
</tr>
</thead>
<tbody>
<tr>
<td>300 mg</td>
<td>14</td>
<td>35</td>
</tr>
<tr>
<td>600 mg</td>
<td>6</td>
<td>7</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Dose</th>
<th>NNT</th>
<th>NNH</th>
</tr>
</thead>
<tbody>
<tr>
<td>300 mg</td>
<td>5</td>
<td>11</td>
</tr>
<tr>
<td>600 mg</td>
<td>4</td>
<td>5</td>
</tr>
</tbody>
</table>

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.

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**BC’s Provincial Academic Detailing (PAD) Service** is offered free of charge to health care professionals. The service is provided by health authorities and supported by the Ministry of Health. Relevant topics are identified in consultation with various groups. All written materials are externally reviewed by clinicians and experts in critical appraisal.
## Medications for Neuropathic Pain: Evidence Brief using the Cochrane Library

### Antiepileptic Medications

<table>
<thead>
<tr>
<th>Medication</th>
<th>Trials</th>
<th>Participants</th>
</tr>
</thead>
<tbody>
<tr>
<td>gabapentin</td>
<td>37</td>
<td>5,914</td>
</tr>
<tr>
<td>pregabalin</td>
<td>45</td>
<td>11,906</td>
</tr>
<tr>
<td>carbamazepine</td>
<td>10</td>
<td>480</td>
</tr>
<tr>
<td>lacosamide</td>
<td>5</td>
<td>1,863</td>
</tr>
<tr>
<td>lamotrigine</td>
<td>12</td>
<td>1,511</td>
</tr>
</tbody>
</table>

### Antidepressant Medications

<table>
<thead>
<tr>
<th>Medication</th>
<th>Trials</th>
<th>Participants</th>
</tr>
</thead>
<tbody>
<tr>
<td>duloxetine</td>
<td>9</td>
<td>2,776</td>
</tr>
<tr>
<td>venlafaxine</td>
<td>6</td>
<td>460</td>
</tr>
<tr>
<td>amitriptyline</td>
<td>17</td>
<td>1,342</td>
</tr>
<tr>
<td>desipramine</td>
<td>5</td>
<td>177</td>
</tr>
<tr>
<td>nortriptyline</td>
<td>6</td>
<td>310</td>
</tr>
</tbody>
</table>

### 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:

- Trials were few in number or small in size (e.g., fewer than 200 participants per treatment arm)
- Short trial durations limit satisfactory assessment of efficacy and safety
- Data on specific benefits (e.g., numbers of people with a substantial reduction in pain) or harms (e.g., 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

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REFERENCES