FREQUENTLY ASKED QUESTIONS
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CCB = calcium channel blocker; NSAID = non-steroidal anti-inflammatory drug
How can neuropathic pain be identified?

Be alert for common verbal descriptors of neuropathic pain:

- Burning
- Tingling
- Shooting
- Electric shock-like
- Numbness

Neuropathic Pain Screening Tools

<table>
<thead>
<tr>
<th>Symptoms</th>
<th>LANSS</th>
<th>DN4</th>
<th>NPQ</th>
<th>painDETECT</th>
<th>ID Pain</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pricking, tingling, pins and needles</td>
<td></td>
<td>X</td>
<td></td>
<td></td>
<td>X</td>
</tr>
<tr>
<td>Electric shocks of shooting</td>
<td>X</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hot or burning</td>
<td></td>
<td></td>
<td>X</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Numbness</td>
<td></td>
<td></td>
<td></td>
<td>X</td>
<td></td>
</tr>
<tr>
<td>Pain evoked by light touch</td>
<td></td>
<td></td>
<td></td>
<td>X</td>
<td></td>
</tr>
<tr>
<td>Clinical examination</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Brush allodynia</td>
<td></td>
<td>X</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Raised soft touch threshold</td>
<td></td>
<td></td>
<td></td>
<td>X</td>
<td></td>
</tr>
<tr>
<td>Altered pin prick threshold</td>
<td></td>
<td>X</td>
<td></td>
<td></td>
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</tr>
</tbody>
</table>

Neuropathic pain screening tools rely largely on common verbal descriptors of pain. Some screening tools also include bedside neurological examination.

Select tool(s) based on ease of use and validation in the local language.

DN4 = Douleur Neuropathique en 4 Questions (DN4) questionnaire; LANSS = Leeds Assessment of Neuropathic Symptoms and Signs; NPQ = Neuropathic Pain Questionnaire

DN4

- Completed by physician in office
- Differentiates neuropathic from nociceptive pain
- 2 pain questions (7 items)
- 2 skin sensitivity tests (3 items)
- Score ≥4 is an indicator for neuropathic pain
- Validated

DN4 = Douleur neuropathique en 4 questions
What is the best non-pharmacological treatment for neuropathic pain?

Various non-pharmacological treatments are available for neuropathic pain and may be discussed with patients. Treatments should be selected based on presumed safety, patient interest and availability.

- Physiotherapy
- Psychotherapy/CBT
- Alternative therapies and spiritual healing
- Patient education

CBT = cognitive behavioral therapy

Evidence for Non-pharmacological Therapies in Neuropathic Pain

- Studied therapies include:
  - Acupuncture
  - Electrostimulation
  - Herbal medicine
  - Magnets
  - Dietary supplements
  - Imagery
  - Spiritual healing

- Limited evidence for most modalities
  - Cannabis extract
  - Carnitine
  - Electrostimulation
  - Magnets

The effectiveness of B vitamins in reducing chronic neuropathic pain has not been established.
What is the most effective way to relieve symptoms of allodynia?

### Drug Selection According to Clinical Presentation

<table>
<thead>
<tr>
<th>Medications</th>
<th>Clinical presentation of neuropathic pain</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Burning</td>
</tr>
<tr>
<td>TCA</td>
<td></td>
</tr>
<tr>
<td>Amitriptyline</td>
<td>++</td>
</tr>
<tr>
<td>SNRI</td>
<td></td>
</tr>
<tr>
<td>Venlafaxine</td>
<td>+</td>
</tr>
<tr>
<td>Duloxetine</td>
<td>++</td>
</tr>
<tr>
<td>Na(^+) channel blockers:</td>
<td></td>
</tr>
<tr>
<td>Carbamazepine</td>
<td>+/-</td>
</tr>
<tr>
<td>Oxcarbazepine</td>
<td>+/-</td>
</tr>
<tr>
<td>Ca(^{2+}) channel (\alpha_2\delta) ligands:</td>
<td></td>
</tr>
<tr>
<td>Gabapentin</td>
<td>++</td>
</tr>
<tr>
<td>Pregabalin</td>
<td>++</td>
</tr>
<tr>
<td>Opioids:</td>
<td></td>
</tr>
<tr>
<td>Tramadol</td>
<td>+</td>
</tr>
<tr>
<td>Morphine</td>
<td>+/-</td>
</tr>
</tbody>
</table>

SNRI = serotonin norepinephrine reuptake inhibitor; TCA = tricyclic antidepressant

Why are nsNSAIDs/coxibs not effective in neuropathic pain?

Coxib = COX-2-specific inhibitor; NSAID = non-steroidal anti-inflammatory drug
nsNSAID = non-specific non-steroidal anti-inflammatory drug

Mechanisms of Neuropathic Pain

There is no target for nsNSAIDs/coxibs to act on in neuropathic pain

What about surgery for neuropathic pain?

• Surgery may be useful in only very select cases:
  – Refractory cases of trigeminal neuralgia
  – Spinal cord stimulation for patients with failed back surgery syndrome and treatment-resistant complex regional pain syndrome

• Neurostimulation may be useful in cases of refractory neuropathic pain, though results appear to be variable

• Surgery is not generally recommended for radiculopathy

When should combination therapy be used for neuropathic pain?

**STEP 1**
Initiate treatment with one or more **first-line** treatments:
- $\alpha_2\delta$ ligands (gabapentin, pregabalin)
- SNRIs ( duloxetine, venlafaxine)
- TCAs* (nortriptyline, desipramine)
- Topical lidocaine (for localized peripheral pain)

**STEP 2**
- If there is partial pain relief, add another first-line medication
- If there is no or inadequate pain relief, switch to another first-line medication

**STEP 3**
If first-line medications alone and in combination fail, consider **second-line** medications (opioids, tramadol) or **third-line** medications (bupropion, citalopram, paroxetine, carbamazepine, lamotrigine, oxcarbazepine, topiramate, valproic acid, topical capsaicin, dextromethorphan, memantine, mexiletine) or referral to pain specialist

*Use tertiary amine TCAs such as amitriptyline only if secondary amine TCAs are unavailable
Note: there is insufficient support for the use of nsNSAIDs in neuropathic pain
nsNSAID = non-specific non-steroidal anti-inflammatory drug; SNRI = serotonin-norepinephrine reuptake inhibitor; TCA = tricyclic antidepressant

How should medications for neuropathic pain be titrated?

<table>
<thead>
<tr>
<th>Medication</th>
<th>Starting dose</th>
<th>Titration</th>
<th>Max. dosage</th>
<th>Trial duration</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>α₂δ ligands</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Gabapentin</td>
<td>100–300 mg at bedtime or tid</td>
<td>↑ by 100–300 mg tid every 1–7 days</td>
<td>3600 mg/day</td>
<td>3–8 weeks + 2 weeks at max. dose</td>
</tr>
<tr>
<td>Pregabalin</td>
<td>50 mg tid or 75 mg bid</td>
<td>↑ to 300 mg/day after 3–7 days, then by 150 mg/day every 3–7 days</td>
<td>600 mg/day</td>
<td>4 weeks</td>
</tr>
<tr>
<td><strong>SNRIs</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Duloxetine</td>
<td>30 mg qd</td>
<td>↑ to 60 mg qd after 1 week</td>
<td>60 mg bid</td>
<td>4 weeks</td>
</tr>
<tr>
<td>Venlafaxine</td>
<td>37.5 mg qd</td>
<td>↑ by 75 mg each week</td>
<td>225 mg/day</td>
<td>4–6 weeks</td>
</tr>
<tr>
<td><strong>TCAs</strong></td>
<td>(desipramine, nortriptyline)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>25 mg at bedtime</td>
<td></td>
<td>↑ by 25 mg/day every 3–7 days</td>
<td>150 mg/day</td>
<td>6–8 weeks, with ≥2 weeks at max.</td>
</tr>
<tr>
<td>Topical lidocaine</td>
<td>Max. 3 5% patches/day for 12 h max.</td>
<td>None needed</td>
<td>Max. 3 patches/day for 12–18 h max.</td>
<td>3 weeks</td>
</tr>
</tbody>
</table>

SNRI = serotonin-norepinephrine reuptake inhibitor; TCA = tricyclic antidepressant
Can you use $\alpha_2\delta$ ligands with CCBs?

- Yes!
  - Unlike CCBs, $\alpha_2\delta$ ligands do not completely block the calcium channel, resulting in virtually no change in systemic blood pressure or coronary blood flow changes.
Can you stop $\alpha_2\delta$ ligands “cold turkey”? 

No!

- Medications should be tapered gradually over at least one week
- Abrupt discontinuation may result in adverse effects, such as insomnia, nausea, headache, and diarrhea