Neuropathic Pain

Introduction
Neuropathic pain is pain due to a lesion, disease or pathological change in the somatosensory (nervous) system. Chronic neuropathic pain is common and may be related to:

- the principal disease or diseases the person has (for example cancer or multiple sclerosis)
- treatment (for example post-operative neuropathic pain or chemotherapy-induced peripheral neuropathy)
- other co-morbid conditions (for example post-herpetic neuralgia or diabetic neuropathy).

It is often complex to manage and may need to be approached differently to standard care with the World Health Organization (WHO) analgesic ladder, so specialist advice should be sought early. Regular review of the patient is essential. Neuropathic pain is commonly found in conjunction with other types of pain.

Assessment

- Refer to Pain Assessment guideline.
- Pain in a dermatomal or neuro-anatomical area, combined with a history of a disease or a lesion that might affect the nervous system, might suggest the possibility of neuropathic pain. This should be confirmed by clinical examination or detailed imaging.
- Sensory descriptors associated with neuropathic pain include burning, tingling, pins and needles, shooting and numbness. These symptoms are not diagnostic.
- Confirm altered sensation in the area of pain by comparing responses with the non-painful contralateral or adjacent area of the body:
  - allodynia – painful response to light touch, for example stroking the skin with a finger or cotton wool
  - hypoaesthesia – an area of reduced sensation to non-painful or painful stimuli
  - hyperalgesia – an exaggerated pain response to stimulus, for example a lowered pin prick threshold
  - altered thermal threshold to cold or hot (for example reduced or exaggerated response to a cold metal spoon, or a hot cup of tea).
- Consider if there is a treatable underlying cause, such as spinal cord compression, and seek specialist advice for further management of the cause.
## Management\(^1\)

<table>
<thead>
<tr>
<th>Medicine</th>
<th>Details</th>
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<tbody>
<tr>
<td><strong>Amitriptyline</strong></td>
<td>- Starting dose: 10mg at night. If tolerated, increase to 25mg after 3 to 7 days, then by 25mg every 1 to 2 weeks.</td>
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<tr>
<td></td>
<td>- Maximum dose 150mg (rarely required or tolerated).</td>
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| **Gabapentin**    | - Starting dose:  
  - titrate from 300mg daily – consider lower starting dose if already on opioids. Refer to British National Formulary (BNF) for further advice.  
  - in elderly or frail patients: 100mg daily. This can be increased by 100mg every 2-3 days as tolerated, up to maximum dose in 3 to 4 divided doses.  
- Maximum licensed dosage for neuropathic pain is 3.6g per day. Specialists may recommend higher doses.  
- Reduce dose in patients with renal impairment and seek specialist advice. |
| **Pregabalin**    | - Starting dose: 25mg twice daily. This can be increased every 2 to 3 days as tolerated up to maximum dose, not exceeding 300mg twice a day.  
- Reduce dose in patients with renal impairment and seek specialist advice. |

## Dosing guidance

- Side effects are common. A low dosage should be used initially particularly in the frail and elderly, and use the lowest dose to achieve analgesia.

## Practice point

- When switching from gabapentin to pregabalin, the following would be reasonable:  
  - replace gabapentin 300mg three times a day with pregabalin 100mg twice a day  
  - replace gabapentin 600mg, 900mg and 1200mg three times a day with pregabalin 200mg twice a day.
- The dose of pregabalin can be further increased, depending on response and tolerability, to a maximum of 300mg twice a day.
- Gabapentin and pregabalin are class C controlled substances. All prescriptions must satisfy controlled drug (CD) prescription requirements to be valid and include details of the dose, form, strength, directions for use and total quantity (in both words and figures).

## General advice

- Opioids have some effect in neuropathic pain, but many patients will need adjuvant analgesics.

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\(^1\)† Indicates this use is off licence  
\(^\text{QT}\) Indicates this medication is associated with QT prolongation
• First-line adjuvants include \textsuperscript{†} tricyclic antidepressants (for example \textsuperscript{QT} amitriptyline) or anticonvulsants (for example gabapentin, usually the first-line anticonvulsant for neuropathic pain; \textsuperscript{QT} pregabalin, occasionally an appropriate first-line option, seek specialist advice). If pain is of mixed origin and not adequately controlled, use conventional analgesics in addition to a tricyclic antidepressant or gabapentin (pregabalin).

• Side effects are common (refer to BNF for a complete list) and include:
  - \textsuperscript{QT} amitriptyline – confusion, hypotension, caution in cardiac disease.
  - gabapentin and \textsuperscript{QT} pregabalin – sedation, tremor, confusion, peripheral oedema, dizziness. Dose reduction is required in patients with renal impairment.

• Alternative second-line adjuvants \textbf{under specialist palliative care advice} include duloxetine\textsuperscript{†} and venlafaxine\textsuperscript{†}. Consider local guidance for drug choice or when changing drugs, for example is there a need for cautious cross-tapering or a washout period (refer to dosing guidance).

• Combining opioids with adjuvants for neuropathic pain is poorly supported by evidence so patients should be regularly reviewed. Skilful titration is needed as side effects (particularly sedation and dizziness) are often synergistic. Only start, or titrate, one drug at a time so that effect and side effects can be attributed accordingly. It is advisable to start with lower doses of both medicines than if they were used as monotherapy, especially in the elderly or if established on opioids.

• Gradually titrate the dose of the analgesic(s) and advise the patient, carer or both of the need for early follow-up. If there is no benefit in pain relief within 8 weeks of titration to the maximal dose tolerated, consider if it is appropriate to reduce and stop. If pain recurs upon reducing, this may imply effect and it may be appropriate to re-titrate.

• Corticosteroids can be used under specialist advice for neuropathic pain secondary to infiltrating cancer, particularly if limb weakness is present. With these symptoms, first consider if further investigation is required urgently to exclude reversible pressure on neurological tissue – refer to \textit{Spinal Cord Compression} guideline. If not, suggested starting dose - dexamethasone\textsuperscript{†} 4mg to 8mg daily for 3-5 days until a benefit is achieved, then reduce to minimum effective dose. If no significant improvement within 5 days, discontinue.

• Specialists may recommend adding \textit{lidocaine plasters}\textsuperscript{†} or topical capsaicin\textsuperscript{†} cream (avoid mucous membranes) for localised pain, particularly if there is allodynia.

• Specialists may recommend other adjuvant analgesics, for example other anticonvulsants (carbamazepine is used for trigeminal neuralgia, but has high incidence of side effects and risk of drug interactions), alternative antidepressants, \textit{ketamine}\textsuperscript{†}, \textsuperscript{QT} \textit{methadone}. 


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• Regular review is essential – seek specialist advice for patients who fail to respond. Specialists may consider early referral for interventional techniques, for example radiotherapy, nerve blocks, epidural or intrathecal analgesia.

• Also consider non-pharmacological interventions for all patients with pain, for example physiotherapy, cognitive behavioural therapy (CBT), transcutaneous electrical nerve stimulation (TENS) or psychological and spiritual support.

• Patients with chronic neuropathic pain should be encouraged to use self-help toolkits for non-pharmacological approaches to pain management.

• Adequate analgesia may take longer in neuropathic pain.

References


