



Therapeutic Brief

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Topic 35: Managing neuropathic pain: a stepwise approach

Neuropathic pain is a very common component of a wide range of pain states, usually resulting from neural damage, including acute and chronic post-operative pain and pain secondary to advanced malignancy. It is a complex condition which often has profound negative physical, psychological and social impacts.

Management is universally acknowledged as extremely challenging,^{1,2} and there is a lack of clear and specific treatment guidelines. Evidence suggests the condition is underdiagnosed and treatment is often sub-optimal which may reflect the complex pathophysiology of neuropathic pain.²⁻⁵

This brief focuses on the therapeutic management of neuropathic pain and highlights the importance of accurate diagnosis, early intervention and regular clinical reviews. It is a guide to treatment options.

Diagnosis and assessment

The aim of diagnosis and assessment is to:

- recognise neuropathic pain
- attempt to ascertain the underlying cause/s
- assess pain and functional limitations due to the pain
- identify comorbidities and possible coexisting depression, anxiety and/or sleep disturbances
- assess the impact of the condition on work, family and social life.²

Appropriate investigation and characterisation of underlying pathology, along with early intervention, is critical to avoid subsequent transition to a chronic pain state.¹

The Australian Immunisation Handbook recommends a single dose of zoster vaccine for people aged 60 years and over who have not previously received a dose, to reduce the symptoms of herpes zoster and the prevalence of post-herpetic neuralgia. (The zoster vaccine has been shown to be less effective in people aged 80 years and over).⁶

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Key points

- Treat early to prevent transition to persistent pain
- Consider a step-wise approach to management:
 - commence with one medicine
 - titrate to attain maximum benefit or maximum dose tolerated
 - allow adequate trial period to assess response
 - if response is inadequate, or side effects experienced, consider changing medicine or adding a new class of medicine
- Conduct regular clinical reviews (include HMRs)
- Refer to specialist or pain clinic if:
 - patient fails to respond to treatment options
 - patient presents with complex pain issues.

Neuropathic pain can be broadly classified as peripheral or central. Box 1 describes some of the many causes of non-malignant neuropathic pain. Because neuropathic pain can be caused by several overlapping disease processes, a patient may experience pain arising from mixed aetiologies including both peripheral and central mechanisms. **It is also possible to experience both nociceptive and neuropathic pain simultaneously.**⁷

Box 1: Some causes of non-malignant neuropathic pain^{1,7,8}

Peripheral disorders
Painful polyneuropathies (diabetic and non-diabetic)
Post-herpetic neuralgia (may have mixed mechanisms)
Trigeminal neuralgia
Brachial plexus injury and limb amputation (phantom limb pain)
Post-surgical and post-traumatic neuralgias
Complex regional pain syndromes
Radiculopathy
Central disorders
Post stroke pain
Spinal cord injury
Multiple sclerosis

Neuropathic pain can be difficult to diagnose as there is no standard diagnostic procedure and laboratory tests do not always identify the cause of pain. A comprehensive evaluation of the patient's history, physical and neurological symptoms (Box 2) and psychosocial issues are the most reliable indicators of the existence and intensity of neuropathic pain.¹ The two following tools may be useful diagnostic aids.

- LANSS (The Leeds Assessment of Neuropathic Symptoms and Signs).⁹ <http://www.londonpainclinic.com/resources/leeds-assessment-of-neuropathic-symptoms-and-signs-lanss/>
- DN 4 (The Douleur Neuropathic en 4) questions.⁹ <http://www.gloshospitals.nhs.uk/en/Wards-and-Departments/>

Box 2: Common symptoms suggestive of neuropathic pain²

Allodynia	Pain initiated or made worse by touch or stimulus that would not normally cause any pain
Hyperalgesia	Severe pain from a stimulus or touch that would normally only cause slight discomfort
Hypoalgesia	Diminished pain or numbness from a painful stimulus
Paresthesia	Pain or discomfort when there is no stimulus or touch at all, can be spontaneous or evoked
Hypoesthesia	An altered tactile or thermal sensitivity – decreased sensitivity to warm or cold objects
Dysesthesia	A spontaneous or evoked abnormal unpleasant sensation

Having your patient complete the S-LANSS Pain Score may provide further valuable information.¹⁰

Principles of care

The principal aim is to improve the patient's quality of life by attaining pain relief whilst minimising adverse drug effects and improving physical function. Measures of physical function may range from basic activities such as walking, eating and grooming, to more complex activities such as shopping, work and leisure/social activities.^{1,11,12}

Many of the drugs used to treat neuropathic pain, including tricyclic antidepressants, gabapentin, pregabalin, duloxetine and opioids are associated with adverse effects that patients find burdensome. These include somnolence, dizziness, motor imbalance and cognitive impairment.^{1,12,13} These adverse effects may significantly restrict the patient's independent living activities, increasing the risk of falls, limiting the ability to drive a car or be actively involved in daily living.

Given the potential individual and unpredictable patient response to these medications, an important aim of care is to consider the efficacy and safety, balanced with the tolerability, especially in elderly and frail people.^{1,11,12}

Global assessment should include pain levels; physical, psychological, environmental and behavioural factors; and patient reports of improvement and satisfaction.¹ It should be undertaken as often as 3 to 4 weekly in response to triggers such as altered pain control, medication adjustment, emergence of possible adverse effects, concerns expressed by patients or other significant alterations in the overall clinical state.

Refer to a pain clinic if your patient fails to respond to treatment or experiences complex pain issues.^{1,11}

Management

Research indicates on average, only half of patients treated with any one modality achieve a clinically significant reduction in pain, and this is not always accompanied by improvement in function.¹⁴ Integrating a combination of treatment modalities is recommended.

Cure and elimination of pain are unlikely. In acknowledging the complex nature of neuropathic pain, discuss with the patient realistic treatment goals and expectations.^{1,11,14} Ensure your patient understands the cause and possible treatments and feels supported. Talk to your patient about concurrent non-pharmacological methods of coping with pain, such as cognitive behavioural and other psychological, physical and occupational therapies.^{11,14}

Approach pharmacological treatment in a step-wise trial and error process that identifies the most appropriate medicine or combination of medicines that provide meaningful pain relief with the least number of adverse effects (see Box 4: Step-wise process).^{1,11} Data are limited on comparative efficacy of medicines used in neuropathic pain and there is no clear choice in treatment.

Simple analgesics, including nonsteroidal anti-inflammatory drugs and paracetamol are usually not effective, unless a component of the pain is due to nociceptive stimulation. Carbamazepine is the first drug of choice for treating trigeminal neuralgia and other atypical facial pain but is not recommended for other neuropathic pain conditions.^{7,8}

The characteristics of individual medicines may impact upon their clinical use.

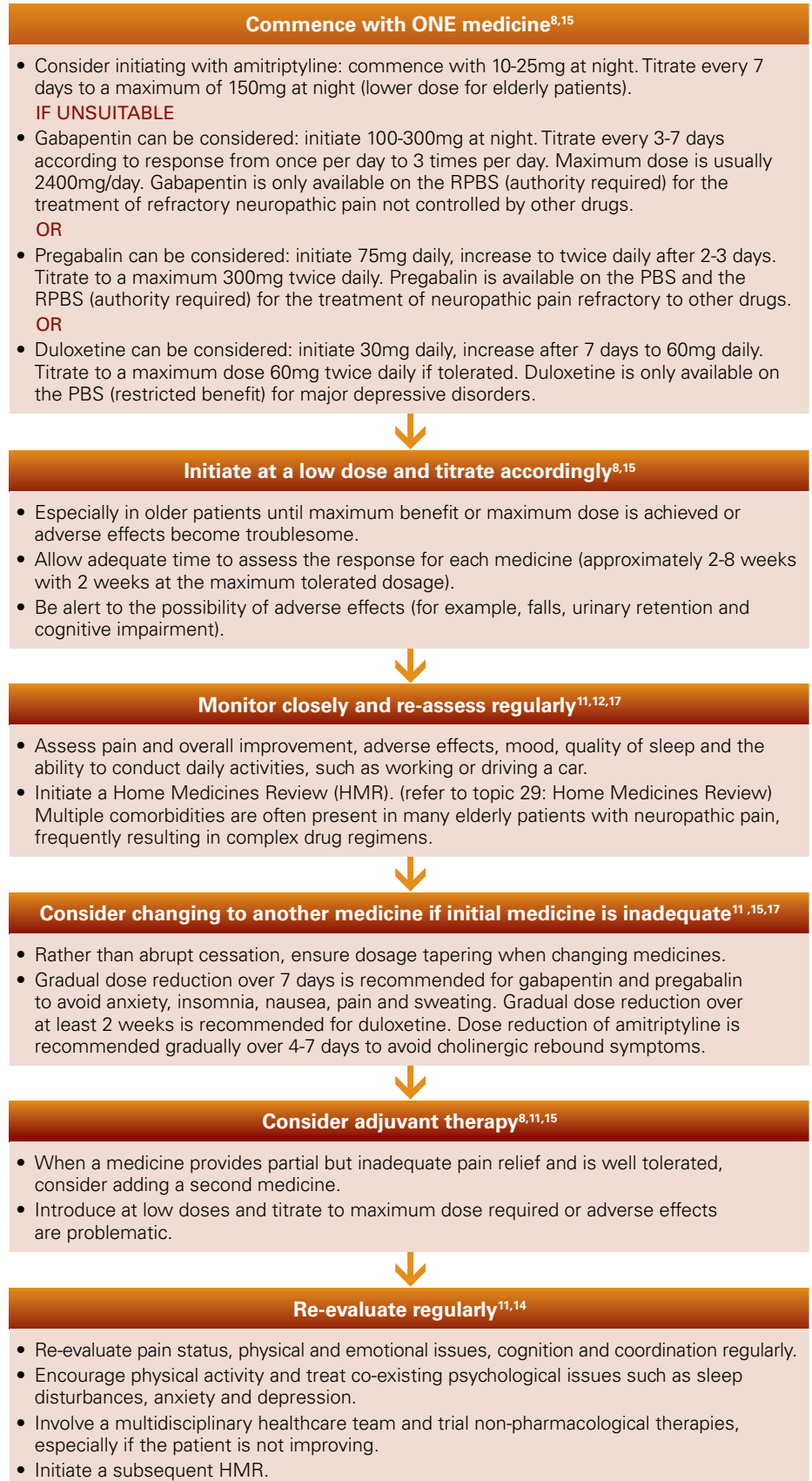
Failure of one medicine to attain pain relief does not mean that others will also fail (even those medicines in the same class). Patient response is often individual and unpredictable, so dose escalation and changing/adding medicines is frequently necessary.^{8,11}

Box 3: Factors to consider when selecting a pain medicine for a given patient¹¹

Efficacy for specific pain type
Tolerability - adverse effects and potential adverse outcomes
Drug interactions – e.g. serotonin toxicity may result when serotonergic agents are used together
Patient comorbidities – e.g. diabetes (renal function)
Patient's ability to adhere to a potentially complex medication regime
Risk of medication abuse*
Risk of intentional or accidental overdose

*Recent reports suggest there is potential for risk of abuse, dependence or withdrawal symptoms with the use of pregabalin and gabapentin. Careful consideration is required when prescribing pregabalin or gabapentin, especially to patients with a history of addictive – related behaviours.¹⁶

Box 4: Step-wise process to follow



Where do opioids fit?

Tramadol and the stronger opioids (morphine, oxycodone and methadone) are not routinely considered as first line treatment options.^{8,18,19} There are concerns about their long term safety relative to the first line treatment options and adverse effects (see Box 5).

Opioids may have a place in pain control in the following: severe disabling neuropathic pain, episodic exacerbations of severe neuropathic pain, and when titrating another medication requiring immediate pain relief is required.¹¹

If pain management is to include opioids, a comprehensive evaluation of the patient including potential risk of abuse/misuse or irregular behaviour in conjunction with close monitoring to gauge efficacy, adverse effects and

Box 5: Adverse effects of regular opioid use

Some common early onset adverse effects of regular opioid use ^{15,18,20}	Some long term adverse effects of regular opioid use ^{15,18,20}
Constipation, nausea and vomiting	Dependence
Drowsiness	Opioid misuse
Impaired cognition	Hypogonadism
Impaired psychomotor function (such as driving a car or playing sport)	Immunologic changes
Respiratory depression	Constipation
Urinary retention	Opioid - induced hyperalgesia ¹¹

improved ability to attend to activities of daily living is recommended.^{1,21} Opioid doses should not exceed the suggested maximum dosage without specialist advice. Withdraw treatment if there is no benefit after a trial of 2-4 weeks. ORT (the Opioid Risk Tool) may be useful in assessing patients.²¹

The paucity of data involving elderly people and the safety of opioids for neuropathic pain control suggests caution in this group. Consider the tolerability profile of opioids if initiating in the elderly or frail as drowsiness, dizziness and motor imbalance can have serious consequences (for example falls and motor vehicle accidents).^{15,20}

References

- Forde G., Martin V. & Stanos S. Pain management dilemmas in primary care. 2007. Available at: http://www.jfponline.com/uploadedFiles/Journal_Site_Files/Journal_of_Family_Practice/supplement_archive/JFPSupp_PainMgmt_0207.pdf [Accessed 9 February 2013].
- International Association for the Study of Pain (IASP). Pain clinical updates September 2010. Available at: <http://www.iasp-pain.org/AM/AMTemplate.cfm?Section=Home&CONTENTID=15084&TEMPLATE=/CM/ContentDisplay.cfm&SECTION=Home> [Accessed 12 January 2013].
- Johnson P., Becker L., Halpern R. et al. Real-world treatment of post-herpetic neuralgia with gabapentin or pregabalin. *Clinical Drug Investigation*. 2013; 33(1): 35-44.
- Berger A., Toelle T., Sadosky A. et al. Clinical and economic characteristics of patients with painful neuropathic disorders in Germany. *Pain Practice*. 2009; 9(1): 8-17.
- Gore M., Duker E., Rowbotham D.J. et al. Clinical characteristics and pain management among patients with pain peripheral neuropathic disorders in general practice settings. *European Journal of Pain*. 2007; 11(6): 652-64.
- The Australian Immunisation Handbook 10th edition. Australian Government. Department of Health and Ageing. 2013. Available at: <http://www.health.gov.au/internet/immunise/publishing.nsf/Content/handbook10-4-24> [Accessed April 2013].
- Australian Pain Society. Evidence-based Recommendations for the Pharmacological Management of Neuropathic Pain. Position Statement, June 2008. Available at: <http://www.fpmx.com.au/pdf/AustPainSoc%20neuropathic%20pain%20guides.pdf> [Accessed 14 January 2013].
- Therapeutic Guidelines: Neurology. Version 4. 2011. Melbourne: Therapeutic Guidelines Ltd.
- Bennett M., Attal N., Backonja M. et al. Using screening tools to identify neuropathic pain. *Pain*. 2007; 127: 199-203.
- Bennett M., Smith B., Torrance N. et al. The S-LANSS Score for identifying pain of predominantly neuropathic origin: validation for use in clinical and postal research. *The Journal of Pain*. 2005; 6 (3): 149-158.
- Dworkin R.H., O'Connor A.B., Backonja M. et al. Pharmacological management of neuropathic pain: Evidence-based recommendations. *Pain* 2007; 132: 237-251.
- Schmader K. E., Baron R., Haanpaa M. et al. Treatment considerations for elderly and frail patients with neuropathic pain. *Mayo Clin Proc* 2010; 85(3) (suppl): S26-S32.
- Quilici S., Chancellor J., Lothgren M. et al. Meta-analysis of duloxetine vs. pregabalin and gabapentin in the treatment of diabetic peripheral neuropathic pain. *BMC Neurology*. 2009; 9(6). Available at: <http://www.biomedcentral.com/1471-2377/9/6> [Accessed 27 February 2013].
- Turk D.C., Wilson H.D. & Cahana A. Treatment of chronic non-cancer pain. *The Lancet*. 2011; 377: 2226-2235.
- Australian Medicines Handbook, Adelaide: Australian Medicines Handbook Pty Ltd 2013.
- No authors listed. Gabapentin and Pregabalin: abuse and addiction. *Adverse Effects*. Translated from *Prescribe Int*. 2012; 21(128): 152 – 154.
- NICE clinical guidelines 96 March 2010. Neuropathic pain: the pharmacological management of neuropathic pain in adults in non-specific settings. Available at: <http://www.nice.org.uk/nicemedia/live/12948/58253/58253.pdf> [Accessed 12 January 2013].
- Dworkin R.H., O'Connor A., Audette J. et al. Recommendations for the pharmacological management of neuropathic pain: an overview and literature update. *Mayo Clin Proc*. 2010; 85(3) (suppl): S3-S14.
- Attal N., Gruccu G., Baron R. et al. EFNS guidelines on the pharmacological treatment of neuropathic pain: 2010 revision. *European Journal of Neurology*. 2010; 17: 1113-1123.
- Pergolizzi J., Boger R., Budd K. et al. Consensus statement: opioids and the management of chronic severe pain in the elderly: consensus statement of an international expert panel with focus on the six clinically most often used world health organisation step III opioids (buprenorphine, fentanyl, hydromorphone, methadone, morphine, oxycodone). *Pain Practice*. 2008; 8(4): 287-313.
- Hunter New England Health Local Health District. Pain Matters: opioid use in persistent pain: Information for health professionals. 2012. Available at: http://www.hnehealth.nsw.gov.au/_data/assets/pdf_file/0016/28141/pmat_neuropathic_Jan_2010.pdf [Accessed April 2013].