NICE National Institute for Health and Care Excellence

NICE guideline

Neuropathic pain in adults: pharmacological management in non-specialist settings

Clinical guideline

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Contents

This guideline replaces CG96.

Introduction

Pain is an unpleasant sensory and emotional experience that can have a significant impact on a person's quality of life, general health, psychological health, and social and economic wellbeing. The International Association for the Study of Pain (IASP 2011) defines neuropathic pain as 'pain caused by a lesion or disease of the somatosensory nervous system'. Central neuropathic pain is defined as 'pain caused by a lesion or disease of the central somatosensory nervous system', and peripheral neuropathic pain is defined as 'pain caused by a lesion or disease of the peripheral somatosensory nervous system'.

Neuropathic pain is very challenging to manage because of the heterogeneity of its aetiologies, symptoms and underlying mechanisms (Beniczky et al. 2005). There is often uncertainty regarding the nature and exact location of a lesion or health condition associated with neuropathic pain, particularly in non-specialist settings. Examples of common conditions that have peripheral neuropathic pain as a symptom are painful diabetic neuropathy, post-herpetic neuralgia, trigeminal neuralgia, radicular pain, post-surgical chronic neuropathic pain, and neuropathic cancer pain (such as, chemotherapy-induced neuropathy, neuropathy secondary to tumour antigens, or caused by direct invasion or compression of neural structures). Examples of conditions that can cause central neuropathic pain include stroke, spinal cord injury and multiple sclerosis. Neuropathic pain can be intermittent or constant, and spontaneous or provoked. Typical descriptions of the pain include terms such as shooting, stabbing, like an electric shock, burning, tingling, tight, numb, prickling, itching and a sensation of pins and needles. People may also describe symptoms of allodynia (pain caused by a stimulus that does not normally provoke pain), hyperalgesia (an increased response to a stimulus that is normally painful), anaesthesia dolorosa (pain felt in an anaesthetic [numb] area or region), and sensory gain or loss (IASP 2011).

A review of the epidemiology of chronic pain found that there is still no accurate estimate available for the population prevalence of neuropathic pain (Smith et al. 2012). For example, the prevalence of neuropathic pain overall has been estimated to be between 6% and 8%, from postal surveys in France (Bouhassira 2008) and the UK (Torrance 2006). However, these estimates came from studies using different questionnaires. Other condition-specific studies have also mirrored the heterogeneous nature of neuropathic pain. For example, painful diabetic neuropathy is estimated to affect between 16% and 26% of people with diabetes (Jensen et al. 2006; Ziegler 2008). Prevalence estimates for post-herpetic neuralgia range from 8% to 19% of people with herpes

zoster when defined as pain at 1 month after rash onset, and 8% when defined as pain at 3 months after rash onset (Schmader 2002).

The development of chronic pain after surgery is also fairly common, with estimates of prevalence ranging from 10% to 50% after many common operations (Shipton 2008). This pain is severe in between 2% and 10% of this subgroup of patients, and many of the clinical features closely resemble those of neuropathic pain (Jung et al. 2004; Mikkelsen et al. 2004; Kehlet et al. 2006). Furthermore, a study of 362,693 computerised records in primary care from the Netherlands estimated the annual incidence of neuropathic pain in the general population to be almost 1% (Dieleman et al. 2008). This considerable variability in estimates of the prevalence and incidence of neuropathic pain and similar conditions from general population studies is likely to be because of differences in the definitions of neuropathic pain, methods of assessment and patient selection (Smith and Torrance 2010, Smith et al. 2012).

A number of pharmacological treatments can be used to manage neuropathic pain outside of specialist pain management services. However, there is considerable variation in how treatment is initiated, the dosages used and the order in which drugs are introduced, whether therapeutic doses are achieved and whether there is correct sequencing of therapeutic classes. A further issue is that a number of commonly used treatments are unlicensed for treating neuropathic pain, which may limit their use. These factors may lead to inadequate pain control, with considerable morbidity.

Commonly used pharmacological treatments include antidepressants (tricyclic antidepressants [TCAs], selective serotonin reuptake inhibitors [SSRIs] and serotonin–norepinephrine reuptake inhibitors [SNRIs]), antiepileptic (anticonvulsant) drugs, topical treatments and opioid analgesics. In addition to their potential benefits, all of these drug classes are associated with various adverse effects.

This short clinical guideline aims to improve the care of adults with neuropathic pain by making evidence-based recommendations on the pharmacological management of neuropathic pain outside of specialist pain management services. A further aim is to ensure that people who require specialist assessment and interventions are referred appropriately and in a timely fashion to a specialist pain management service and/or other condition-specific services.

Drug recommendations

For all drugs, recommendations are based on evidence of clinical and cost effectiveness and reflect whether their use for the management of neuropathic pain is a good use of NHS resources. This

guideline should be used in conjunction with clinical judgement and decision-making appropriate for the individual patient.

The guideline will assume that prescribers will use a drug's summary of product characteristics (SPC) and the British National Formulary (BNF) to inform decisions made with individual patients (this includes obtaining information on special warnings, precautions for use, contraindications and adverse effects of pharmacological treatments).

This guideline recommends some drugs for indications for which they do not have a UK marketing authorisation at the date of publication, if there is good evidence to support that use. The prescriber should follow relevant professional guidance, taking full responsibility for the decision. The patient (or those with authority to give consent on their behalf) should provide informed consent, which should be documented. See the General Medical Council's Good practice in prescribing and managing medicines and devices (2013). Where recommendations have been made for the use of drugs outside their licensed indications (off-label use), these drugs are marked with a footnote in the recommendations.

Healthcare setting for this guideline

The recommendations in this clinical guideline are for the pharmacological management of neuropathic pain in non-specialist settings only. The Guideline Development Group acknowledged that there are other pharmacological and non-pharmacological treatments that will be of benefit to people with neuropathic pain, within different care pathways in different settings.

The following definitions apply to this guideline.

Non-specialist settings are primary and secondary care services that do not provide specialist pain services. Non-specialist settings include general practice, general community care and hospital care.

Specialist pain services are those that that provide comprehensive assessment and multi-modal management of all types of pain, including neuropathic pain.

Patient-centred care

This guideline offers best practice advice on the care of adults with neuropathic pain who are treated outside specialist pain management services.

Patients and healthcare professionals have rights and responsibilities as set out in the NHS Constitution for England – all NICE guidance is written to reflect these. Treatment and care should take into account individual needs and preferences. Patients should have the opportunity to make informed decisions about their care and treatment, in partnership with their healthcare professionals. If the patient is under 16, their family or carers should also be given information and support to help the child or young person to make decisions about their treatment. Healthcare professionals should follow the Department of Health's advice on consent. If someone does not have capacity to make decisions, healthcare professionals should follow the code of practice that accompanies the Mental Capacity Act and the supplementary code of practice on deprivation of liberty safeguards. In Wales, healthcare professionals should follow advice on consent from the Welsh Government.

NICE has produced guidance on the components of good patient experience in adult NHS services. All healthcare professionals should follow the recommendations in Patient experience in adult NHS services.

1 Recommendations

The following guidance is based on the best available evidence. The full guideline gives details of the methods and the evidence used to develop the guidance.

> The wording used in the recommendations in this guideline (for example, words such as 'offer' and 'consider') denotes the certainty with which the recommendation is made (the strength of the recommendation). See About this guideline for details.

1.1 List of all recommendations

Key principles of care

1.1.1 When agreeing a treatment plan with the person, take into account their concerns and expectations, and discuss:

- the severity of the pain, and its impact on lifestyle, daily activities (including sleep disturbance) and participation[a]
- the underlying cause of the pain and whether this condition has deteriorated
- why a particular pharmacological treatment is being offered
- the benefits and possible adverse effects of pharmacological treatments, taking into account any physical or psychological problems, and concurrent medications
- the importance of dosage titration and the titration process, providing the person with individualised information and advice
- coping strategies for pain and for possible adverse effects of treatment
- non-pharmacological treatments, for example, physical and psychological therapies (which may be offered through a rehabilitation service) and surgery (which may be offered through specialist services).

  For more information about involving people in decisions and supporting adherence, see Medicines adherence (NICE clinical guideline 76).

1.1.2 Consider referring the person to a specialist pain service and/or a condition-specific service[2] at any stage, including at initial presentation and at the regular clinical reviews (see recommendation 1.1.6), if:

- they have severe pain **or**
- their pain significantly limits their lifestyle, daily activities (including sleep disturbance) and participation[1] **or**
- their underlying health condition has deteriorated.

1.1.3 Continue existing treatments for people whose neuropathic pain is already effectively managed, taking into account the need for regular clinical reviews (see recommendation 1.1.6).

1.1.4 When introducing a new treatment, take into account any overlap with the old treatments to avoid deterioration in pain control.

1.1.5 After starting or changing a treatment, carry out an early clinical review of dosage titration, tolerability and adverse effects to assess the suitability of the chosen treatment.

1.1.6 Carry out regular clinical reviews to assess and monitor the effectiveness of the treatment. Each review should include an assessment of:

- pain control
- impact on lifestyle, daily activities (including sleep disturbance) and participation[1]
- physical and psychological wellbeing
- adverse effects
- continued need for treatment.

1.1.7 When withdrawing or switching treatment, taper the withdrawal regimen to take account of dosage and any discontinuation symptoms.

Treatment

All neuropathic pain (except trigeminal neuralgia)

1.1.8 Offer a choice of amitriptyline, duloxetine, gabapentin or pregabalin as initial treatment for neuropathic pain (except trigeminal neuralgia)[3].

1.1.9 If the initial treatment is not effective or is not tolerated, offer one of the remaining 3 drugs, and consider switching again if the second and third drugs tried are also not effective or not tolerated.

1.1.10 Consider tramadol only if acute rescue therapy is needed (see recommendation 1.1.12 about long-term use).

1.1.11 Consider capsaicin cream[4] for people with localised neuropathic pain who wish to avoid, or who cannot tolerate, oral treatments.

Treatments that should not be used

1.1.12 Do not start the following to treat neuropathic pain in non-specialist settings, unless advised by a specialist to do so:

- cannabis sativa extract
- capsaicin patch
- lacosamide
- lamotrigine
- levetiracetam
- morphine
- oxcarbazepine
- topiramate
- tramadol (this is referring to long-term use; see recommendation 1.1.10 for short-term use)
- venlafaxine.

Trigeminal neuralgia

1.1.13 Offer carbamazepine as initial treatment for trigeminal neuralgia.

1.1.14 If initial treatment with carbamazepine is not effective, is not tolerated or is contraindicated, consider seeking expert advice from a specialist and consider early referral to a specialist pain service or a condition-specific service.

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[1] The World Health Organization ICF (International Classification of Functioning, Disability and Health) (2001) defines participation as 'A person's involvement in a life situation.' It includes the following domains: learning and applying knowledge, general tasks and demands, mobility, self-care, domestic life, interpersonal interactions and relationships, major life areas, community, and social and civil life.

[2] A condition-specific service is a specialist service that provides treatment for the underlying health condition that is causing neuropathic pain. Examples include neurology, diabetology and oncology services.

[3] At the time of publication (November 2013), amitriptyline did not have a UK marketing authorisation for this indication, duloxetine is licensed for diabetic peripheral neuropathic pain only, and gabapentin is licensed for peripheral neuropathic pain only, so use for other conditions would be off-label. In addition, the Lyrica (Pfizer) brand of pregabalin has patent protection until July 2017 for its licensed indication of treatment of peripheral and central neuropathic pain; until such time as this patent expires generic pregabalin products will not be licensed for this indication and their use for this condition would be off-label and may infringe the patent. The prescriber should follow relevant professional guidance, taking full responsibility for the decision. Informed consent should be obtained and documented. See the General Medical Council's Good practice in prescribing and managing medicines and devices for further information.

[4] At the time of publication (November 2013), capsaicin cream (Axsain) had a UK marketing authorisation for post-herpetic neuralgia and painful diabetic peripheral polyneuropathy, so use for other conditions would be off-label. The SPC states that this should only be used for painful diabetic peripheral polyneuropathy 'under the direct supervision of a hospital consultant who has access to specialist resources'. The prescriber should follow relevant professional guidance, taking full responsibility for the decision. Informed consent should be obtained and documented. See the General Medical Council's Good practice in prescribing and managing medicines and devices for further information.

2 List of all research recommendations

The Guideline Development Group has made the following recommendations for research, based on its review of evidence, to improve NICE guidance and patient care in the future.

2.1 Monotherapy versus combination therapy for treating neuropathic pain

What is the clinical effectiveness, cost effectiveness and tolerability of pharmacological monotherapy compared with combination therapy for treating neuropathic pain?

Why this is important

Combination therapy is commonly prescribed for neuropathic pain. It may also be a helpful option as a stepwise approach if initially used drugs are insufficient at reducing pain. Combination therapy may also result in better tolerability because smaller doses of individual drugs are often used when combined with other drugs. However, there is a lack of trial evidence comparing the clinical and cost effectiveness and tolerability of different drug combinations. Further research should be conducted as described in the table below.

Criterion	Explanation

Population	Adults with a diagnosis of neuropathic pain. Neuropathic pain conditions include: • Central neuropathic pain/central pain • Complex regional pain syndromes • Compression neuropathies/nerve compression syndromes • Facial neuralgia • HIV-related neuropathy • Mixed neuropathic pain • Multiple sclerosis • Neurogenic pain • Neuropathic cancer pain/cancer pain • Neuropathic pain • Painful diabetic neuropathy/diabetic neuropathy • Peripheral nerve injury • Peripheral nervous system disease/neuropathies • Phantom limb pain • Polyneuropathies • Post-amputation pain • Post-herpetic neuralgia • Post-stroke pain • Post-treatment/post-surgery/post-operative pain • Radiculopathies/radicular pain • Spinal cord diseases

	• Spinal cord injury • Trigeminal neuralgia

Intervention(s)	Pharmacological agents as monotherapy or combination therapy. The pharmacological agents include: • Amitriptyline • Clomipramine • Dosulepin (dothiepin) • Doxepin • Imipramine • Lofepramine • Nortriptyline • Trimipramine • Citalopram • Escitalopram • Fluoxetine • Paroxetine • Sertraline • Duloxetine • Mirtazapine • Reboxetine • Trazodone • Venlafaxine • Carbamazepine • Gabapentin • Lacosamide

	• Lamotrigine • Levetiracetam • Oxcarbazepine • Phenytoin • Pregabalin • Valproate • Topiramate • Buprenorphine • Co-codamol • Co-dydramol • Dihydrocodeine • Fentanyl • Morphine • Oxycodone • Oxycodone with naloxone • Tapentadol • Tramadol • Cannabis sativa extract • Flecainide • 5-HT_1-receptor agonists • Topical capsaicin • Topical lidocaine

Comparator(s)	Any of the above listed pharmacological agents as monotherapy compared with any combinations of the above listed pharmacological agents as combination therapy.
Outcome(s)	Patient-reported global improvement (on a 7-point scale) Patient-reported improvement in daily physical and emotional functioning including sleep (on a 9-point scale) At least 30% and 50% pain reduction (on a 11-point Numerical rating scale [NRS] scale) Mean change from baseline pain scores (on a 11-NRS scale) Withdrawal due to adverse effects of the pharmacological agents Adverse effects of the pharmacological agents HRQoL (for example, EQ-5D, WHOQoL- BREF and London Handicap Scale)
Study design	Parallel triple-blinded randomised controlled trial of at least 12-weeks' study period (they should not have enriched enrolment). All participants should have a 'wash-out' period after assessment for inclusion in the study and before randomisation. Baseline pain scores between arms should be equal and clearly documented. Concomitant medications should not be allowed or should be restricted and maintained at a stable dose in the study. Difference in concomitant pain medication usage at baseline should be clearly described in each trial arm, including details of the number of patients on different drugs. Rescue pain medications should either not be allowed or, if used, their use should be accurately documented.

2.2 Relationship between symptoms, cause of neuropathic pain and its treatment

Is response to pharmacological treatment predicted more reliably by underlying aetiology or by symptom characteristics?

Why this is important

There is little evidence about whether certain symptoms that present in healthcare settings, or whether different neuropathic pain conditions with different aetiologies, respond differently to

different treatments. Current evidence is typically focused on particular conditions and is limited to particular drugs. Further research should be conducted as described in the table below.

Criterion	Explanation

Population	Adults with a diagnosis of neuropathic pain. Neuropathic pain conditions include: • Central neuropathic pain/central pain • Complex regional pain syndromes • Compression neuropathies/nerve compression syndromes • Facial neuralgia • HIV-related neuropathy • Mixed neuropathic pain • Multiple sclerosis • Neurogenic pain • Neuropathic cancer pain/cancer pain • Neuropathic pain • Painful diabetic neuropathy/diabetic neuropathy • Peripheral nerve injury • Peripheral nervous system disease/neuropathies • Phantom limb pain • Polyneuropathies • Post-amputation pain • Post-herpetic neuralgia • Post-stroke pain • Post-treatment/post-surgery/post-operative pain • Radiculopathies/radicular pain • Spinal cord diseases

	• Spinal cord injury • Trigeminal neuralgia
Intervention(s)	Any pharmacological agents as monotherapy or combination therapy (see research recommendation B1).
Comparator(s)	Same pharmacological agents chosen as the main treatments of interest but compare the treatment response across different groups of participants with different neuropathic pain conditions or underlying aetiology.
Outcome(s)	Patient-reported global improvement (on a 7-point scale) Patient-reported improvement in daily physical and emotional functioning including sleep (on a 9-point scale) At least 30% and 50% pain reduction (on a 11-NRS scale) Mean change from baseline pain scores (on a 11-NRS scale) Withdrawal due to adverse effects of the pharmacological agents Adverse effects of the pharmacological agents HRQoL (for example, EQ-5D, WHOQoL- BREF and London Handicap Scale)
Study design	Prospective cohort study All participants should have a 'wash-out' period before assessment for inclusion in the study. Baseline pain scores between arms should be equal and clearly documented. Concomitant medications should not be allowed, or should be restricted and maintained at stable dose during the study. Difference in concomitant pain medication usage at baseline should be clearly described in each trial arm, including details of the number of patients on different drugs. Rescue pain medications either not be allowed or, if used, their use should be accurately documented.

2.3 Carbamazepine for treating trigeminal neuralgia

What is the clinical and cost effectiveness of carbamazepine as initial treatment for trigeminal neuralgia compared with other pharmacological treatments?

Why this is important

Carbamazepine has been the standard treatment for trigeminal neuralgia since the 1960s. Despite the lack of trial evidence, it is perceived by clinicians to be efficacious. Further research should be conducted as described in the table below.

Criterion	Explanation
Population	Adults with a diagnosis of trigeminal neuralgia.
Intervention(s)	Carbamazepine as monotherapy.

Comparator(s)	Any of the below listed pharmacological agents as monotherapy or combinations. The pharmacological agents include: • Amitriptyline • Clomipramine • Dosulepin (dothiepin) • Doxepin • Imipramine • Lofepramine • Nortriptyline • Trimipramine • Citalopram • Escitalopram • Fluoxetine • Paroxetine • Sertraline • Duloxetine • Mirtazapine • Reboxetine • Trazodone • Venlafaxine • Carbamazepine • Gabapentin • Lacosamide

	• Lamotrigine • Levetiracetam • Oxcarbazepine • Phenytoin • Pregabalin • Valproate • Topiramate • Buprenorphine • Co-codamol • Co-dydramol • Dihydrocodeine • Fentanyl • Morphine • Oxycodone • Oxycodone with naloxone • Tapentadol • Tramadol • Cannabis sativa extract • Flecainide • 5-HT_1-receptor agonists • Topical capsaicin • Topical lidocaine

Outcome(s)	Patient-reported global improvement (on a 7-point scale) Patient-reported improvement in daily physical and emotional functioning including sleep (on a 9-point scale) At least 30% and 50% pain reduction (on a 11-NRS scale) Mean change from baseline pain scores (on a 11-NRS scale) Withdrawal due to adverse effects of the pharmacological agents Adverse effects of the pharmacological agents HRQoL (for example, EQ-5D, WHOQoL- BREF and London Handicap Scale)
Study design	Parallel triple-blinded randomised controlled trial of at least 12 weeks' study period (they should not have enriched enrolment). All participants should have a 'wash-out' period after assessment for inclusion in the study and before randomisation. Baseline pain scores between arms should be equal and clearly documented. Concomitant medications should not be allowed or should be restricted and maintained at a stable dose during the study. Difference in concomitant pain medication usage at baseline should be clearly described in each trial arm, including details of the number of patients on different drugs. Rescue pain medications either not be allowed or, if used, their use should be accurately documented.

2.4 Factors affecting participation and quality of life

What are the key factors, including additional care and support, that influence participation[5] and quality of life in people with neuropathic pain?

Why this is important

There is evidence suggesting that people with neuropathic pain experience poorer physical and mental health than people with other forms of pain, even when adjusted for pain intensity. The discrepancy between pain intensity and quality of life implies that other, unrecognisable factors are important for people with neuropathic pain and that these factors may influence their daily activities and participation. Further research should be conducted as described in the table below.

Criterion	Explanation

Population	Adults with a diagnosis of neuropathic pain. Neuropathic pain conditions include: • Central neuropathic pain/central pain • Complex regional pain syndromes • Compression neuropathies/nerve compression syndromes • Facial neuralgia • HIV-related neuropathy • Mixed neuropathic pain • Multiple sclerosis • Neurogenic pain • Neuropathic cancer pain/cancer pain • Neuropathic pain • Painful diabetic neuropathy/diabetic neuropathy • Peripheral nerve injury • Peripheral nervous system disease/neuropathies • Phantom limb pain • Polyneuropathies • Post-amputation pain • Post-herpetic neuralgia • Post-stroke pain • Post-treatment/post-surgery/post-operative pain • Radiculopathies/radicular pain • Spinal cord diseases

	• Spinal cord injury • Trigeminal neuralgia
Intervention(s)	Any important factors, including elements of additional care and support that are perceived as important by adults with neuropathic pain to improve their daily participation.
Comparator(s)	Non-applicable.
Outcome(s)	HRQoL (for example, EQ-5D, WHOQoL- BREF) Measurements of participation (for example, the London Handicap Scale) Satisfaction Patient experiences
Study design	Qualitative research or structured/semi-structured survey questionnaire.

2.5 Impact of drug-related adverse effects on cost effectiveness and quality of life

What is the impact of drug-related adverse effects on health economics and quality of life in neuropathic pain?

Why this is important

Pharmacological agents for neuropathic pain are associated with various adverse effects. However, there is little evidence about how this affects cost of the quality of life of patients receiving treatment. Further research should be conducted as described in the table below.

Criterion	Explanation

Population	Adults with a diagnosis of neuropathic pain. Neuropathic pain conditions include: • Central neuropathic pain/central pain • Complex regional pain syndromes • Compression neuropathies/nerve compression syndromes • Facial neuralgia • HIV-related neuropathy • Mixed neuropathic pain • Multiple sclerosis • Neurogenic pain • Neuropathic cancer pain/cancer pain • Neuropathic pain • Painful diabetic neuropathy/diabetic neuropathy • Peripheral nerve injury • Peripheral nervous system disease/neuropathies • Phantom limb pain • Polyneuropathies • Post-amputation pain • Post-herpetic neuralgia • Post-stroke pain • Post-treatment/post-surgery/post-operative pain • Radiculopathies/radicular pain • Spinal cord diseases

	• Spinal cord injury • Trigeminal neuralgia
Intervention(s)	Any pharmacological treatment for neuropathic pain, alone or in combination (see research recommendation B1)
Comparator(s)	N/A
Outcome(s)	HRQoL (EQ-5D as well as any condition-specific instruments) in people experiencing adverse effects and people experiencing none Resource-use and costs in people experiencing adverse effects and people experiencing none
Study design	Case–control study This research should be performed in a cohort of people receiving a variety of pharmacological treatments for neuropathic pain. Those experiencing adverse effects should be matched with those experiencing none, and their HRQoL and resource-use/costs compared. Matching should be performed using as many modifiers of HRQoL as possible, including age, sex and underlying diagnosis. Analysis of single, named adverse events and also of people experiencing any serious adverse effect (those leading to discontinuation of the medication in question) would be valuable.

2.6 Potential for dependence associated with pharmacological drugs for neuropathic pain

Is there a potential for dependence associated with pharmacological agents for neuropathic pain?

Why this is important

There has been some suggestion that some pharmacological agents for neuropathic pain are associated with increased potential for misuse. However, there had not been enough high-quality evidence to adequately explore this issue. Further research should be conducted as described in the table below.

Criterion	Explanation

Population	Adults with a diagnosis of neuropathic pain. Neuropathic pain conditions include: • Central neuropathic pain/central pain • Complex regional pain syndromes • Compression neuropathies/nerve compression syndromes • Facial neuralgia • HIV-related neuropathy • Mixed neuropathic pain • Multiple sclerosis • Neurogenic pain • Neuropathic cancer pain/cancer pain • Neuropathic pain • Painful diabetic neuropathy/diabetic neuropathy • Peripheral nerve injury • Peripheral nervous system disease/neuropathies • Phantom limb pain • Polyneuropathies • Post-amputation pain • Post-herpetic neuralgia • Post-stroke pain • Post-treatment/post-surgery/post-operative pain • Radiculopathies/radicular pain • Spinal cord diseases

	• Spinal cord injury • Trigeminal neuralgia
Intervention(s)	Any pharmacological treatment for neuropathic pain, alone or in combination (see research recommendation B1)
Comparator(s)	Any other pharmacological treatment for neuropathic pain, alone or in combination (see research recommendation B1)
Outcome(s)	Drug dependence (including withdrawal symptoms) Drug abuse or drug misuse
Study design	Long-term follow-up from a randomised controlled trial (minimum 6 months) or community-based observational studies. For trials: • Intention to observe dependency and misuse should be made in the study protocol and monitored throughout the study period. • All participants should have a 'wash-out' period after assessment for inclusion in the study and before randomisation. • Baseline pain scores between arms should be equal and clearly documented. • Concomitant medications should not be allowed or should be restricted and maintained at a stable dose in the study. Difference in concomitant pain medication usage at baseline should be clearly described in each trial arm, including details of the number of patients on different drugs. • Rescue pain medications should either not be allowed or, if used, their use should be accurately documented.

[5] The World Health Organization ICF (International Classification of Functioning, Disability and Health) (2001) defines participation as 'A person's involvement in a life situation.' It includes the following domains: learning and applying knowledge, general tasks and demands, mobility, self-care, domestic life, interpersonal interactions and relationships, major life areas, community, and social and civil life.

3 Other information

3.1 Scope and how this guideline was developed

NICE guidelines are developed in accordance with a scope that defines what the guideline will and will not cover.

3.2 Related NICE guidance

Further information is available on the NICE website.

Published

General

- Patient experience in adult NHS services. NICE clinical guidance 138 (2012).
- Medicines adherence. NICE clinical guidance 76 (2011).

Condition-specific

- Opioids in palliative care. NICE clinical guideline 140 (2012)
- Low back pain. NICE clinical guideline 88 (2009).
- Multiple sclerosis. NICE clinical guideline 8 (2003).

Under development

NICE is developing the following guidance (details available from the NICE website):

- Type 1 diabetes (update). NICE clinical guideline. Publication date to be confirmed.
- Type 2 diabetes (update). NICE clinical guideline. Publication date to be confirmed.

4 The Guideline Development Group and NICE project team

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4.5 Acknowledgements

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Changes after publication

December 2014: amended footnote to recommendation 1.1.8 to clarify use of generic pregabalin and off-label status.

About this guideline

NICE clinical guidelines are recommendations about the treatment and care of people with specific diseases and conditions in the NHS in England and Wales.

NICE guidelines are developed in accordance with a scope that defines what the guideline will and will not cover.

This guideline was developed by the NICE Internal Clinical Guidelines Programme. The Internal Clinical Guidelines Programme worked with a Guideline Development Group, comprising healthcare professionals (including consultants, GPs and nurses), patients and carers, and technical staff, which reviewed the evidence and drafted the recommendations. The recommendations were finalised after public consultation.

The methods and processes for developing NICE clinical guidelines are described in The guidelines manual. This guideline was developed using the short clinical guideline process.

Update information

This guidance is an update of NICE clinical guideline 96 (published March 2010) and replaces it.

Strength of recommendations

Some recommendations can be made with more certainty than others. The Guideline Development Group makes a recommendation based on the trade-off between the benefits and harms of an intervention, taking into account the quality of the underpinning evidence. For some interventions, the Guideline Development Group is confident that, given the information it has looked at, most patients would choose the intervention. The wording used in the recommendations in this guideline denotes the certainty with which the recommendation is made (the strength of the recommendation).

For all recommendations, NICE expects that there is discussion with the patient about the risks and benefits of the interventions, and their values and preferences. This discussion aims to help them to reach a fully informed decision (see also Patient-centred care).

Interventions that must (or must not) be used

We usually use 'must' or 'must not' only if there is a legal duty to apply the recommendation. Occasionally we use 'must' (or 'must not') if the consequences of not following the recommendation could be extremely serious or potentially life threatening.

Interventions that should (or should not) be used – a 'strong' recommendation

We use 'offer' (and similar words such as 'refer' or 'advise') when we are confident that, for the vast majority of patients, an intervention will do more good than harm, and be cost effective. We use similar forms of words (for example, 'Do not offer…') when we are confident that an intervention will not be of benefit for most patients.

Interventions that could be used

We use 'consider' when we are confident that an intervention will do more good than harm for most patients, and be cost effective, but other options may be similarly cost effective. The choice of intervention, and whether or not to have the intervention at all, is more likely to depend on the patient's values and preferences than for a strong recommendation, and so the healthcare professional should spend more time considering and discussing the options with the patient.

Other versions of this guideline

The full guideline, Neuropathic pain – pharmacological management: the pharmacological management of neuropathic pain in adults in non-specialist settings, contains details of the methods and evidence used to develop the guideline. It is published by the Internal Clinical Guidelines Programme.

The recommendations from this guideline have been incorporated into a NICE Pathway.

We have produced information for the public about this guideline.

Implementation

Implementation tools and resources to help you put the guideline into practice are also available.

Your responsibility

This guidance represents the view of NICE, which was arrived at after careful consideration of the evidence available. Healthcare professionals are expected to take it fully into account when exercising their clinical judgement. However, the guidance does not override the individual responsibility of healthcare professionals to make decisions appropriate to the circumstances of the individual patient, in consultation with the patient and/or guardian or carer, and informed by the summaries of product characteristics of any drugs.

Implementation of this guidance is the responsibility of local commissioners and/or providers. Commissioners and providers are reminded that it is their responsibility to implement the guidance, in their local context, in light of their duties to have due regard to the need to eliminate unlawful discrimination, advance equality of opportunity and foster good relations. Nothing in this guidance should be interpreted in a way that would be inconsistent with compliance with those duties.

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