

Appendix C Guideline scope

NATIONAL INSTITUTE FOR HEALTH AND CLINICAL EXCELLENCE

SCOPE

1 Guideline title

Neuropathic pain – pharmacological management: the pharmacological management of neuropathic pain in adults in non-specialist settings

1.1 Short title

Neuropathic pain – pharmacological management

2 The remit

The Department of Health has asked NICE: 'To prepare a short clinical guideline on the pharmacological management of neuropathic pain in adults, in non-specialist settings.' [Update]

3 Clinical need for the guideline

3.1 Epidemiology

- a) Neuropathic pain refers to pain caused by a lesion or disease of the somatosensory nervous system. This can result from a heterogeneous group of disorders affecting the peripheral and central nervous systems. Common examples of peripheral neuropathic pain include painful diabetic neuropathy, post-herpetic neuralgia, radiculopathy, and trigeminal neuralgia. Common examples of central neuropathic pain include multiple sclerosis, pain after stroke and after spinal cord injury.
- b) The main clinical features of neuropathic pain are continuous or intermittent spontaneous pain, typically described as burning, aching or shooting in quality. It is an unpleasant sensory and

emotional experience and can have a significant impact on the quality of life, general health, psychological health, and social and economic wellbeing of people with neuropathic pain.

- c) Neuropathic pain is an important cause of chronic pain and commonly occurs in people with diabetes and following herpes zoster infection. Neuropathic pain is diagnosed and managed in primary care and secondary care as well as by specialist pain management services (services that provide comprehensive assessment and multi-modal management of all types of pain, including neuropathic pain). However, there is limited evidence on the incidence and prevalence of neuropathic pain outside of specialist pain management services. A descriptive epidemiological study of neuropathic pain in a UK general practice population shows that post-herpetic neuralgia has the highest incidence (40 per 100,000 person years observation) followed by trigeminal neuralgia (27 per 100,000 person years observation) and painful diabetic neuropathy (15 per 100,000 person years observation). This is likely to be an underestimate because not all cases will have been correctly identified.
- d) There is also evidence that the incidence of post-herpetic neuralgia and painful diabetic neuropathy increases with age and, in the case of the latter, the duration of diabetes.

3.2 *Current practice*

- a) Several pharmacological treatments are commonly used to manage neuropathic pain outside of specialist pain management services. These include antidepressants (tricyclic antidepressants [TCAs] and selective serotonin reuptake inhibitors [SSRIs]) and anti-epileptic drugs (such as gabapentin, pregabalin and carbamazepine). Topical agents (capsaicin and lidocaine) can also be used. Opioids can also be used to treat neuropathic pain, but not all neuropathic pain is opioid-responsive. The use of strong opioids for treating non-malignant chronic pain conditions is

controversial because of concerns about the long-term side effect profile of the drugs. Some commonly used treatments (such as amitriptyline) are unlicensed for use in neuropathic pain, which may limit prescription by practitioners. There is uncertainty about which drugs should be used for neuropathic pain, and in what order (sequence).

- b) There is evidence that neuropathic pain is commonly managed in primary care and other settings outside of specialist pain management services. However, there is considerable variation in practice in terms of how therapy is initiated, whether therapeutic doses are achieved, the concomitant use of different drugs, and whether the different types of drugs are used in the correct sequence. This may lead to inadequate pain control and considerable morbidity. Better management of neuropathic pain in non-specialist settings could not only reduce such variation but also ensure that only those people who need specialist assessment and interventions are referred on.

4 The guideline

The guideline development process is described in detail on the NICE website (see section 6, 'Further information').

This scope defines what the guideline will (and will not) examine, and what the guideline developers will consider. The scope is based on the referral from the Department of Health.

The areas that will be addressed by the guideline are described in the following sections.

4.1 Population

4.1.1 Groups that will be covered

- a) Adults with neuropathic pain.

4.1.2 Groups that will not be covered

- a) Children and young people with neuropathic pain.

4.2 Settings

4.2.1 Healthcare settings that will be covered

- a) All settings where care is delivered for NHS patients, except specialist pain management services.

4.2.2 Healthcare settings that will not be covered

- a) Specialist pain management services.

4.3 Clinical management

4.3.1 Key clinical issues that will be covered

- a) Use of the drug therapeutic classes detailed below, and their positioning within the care pathway for the management of neuropathic pain outside of specialist pain management services. This will include use of individual drugs as monotherapy and/or in combination, if clearly supported by evidence.
- b) Note that guideline recommendations will normally fall within licensed indications; recommendations outside of a licensed indication may be made but only if clearly supported by the evidence. The guideline will assume that prescribers will use a drug's summary of product characteristics to inform decisions made with individual patients. It is noted that a number of drugs are used for neuropathic pain that do not have a UK marketing authorisation (licence) for this use and so are considered to be used 'off-label'. This is indicated in the text.
- c) The following antidepressants will be considered:
 - Tricyclic antidepressants (TCAs):
 - amitriptyline (off-label use)
 - clomipramine (off-label use)

- dosulepin (off-label use)
- doxepin (off-label use)
- imipramine (off-label use)
- lofepramine (off-label use)
- nortriptyline (off-label use)
- trimipramine (off-label use).
- Selective serotonin reuptake inhibitors (SSRIs):
 - citalopram (off-label use)
 - escitalopram (off-label use)
 - fluoxetine (off-label use)
 - paroxetine (off-label use)
 - sertraline (off-label use).
- Other antidepressants:
- duloxetine (licensed for diabetic peripheral neuropathic pain only)
 - mirtazapine (off-label use)
 - reboxetine (off-label use)
 - trazodone (off-label use)
 - venlafaxine (off-label use).

d) The following anti-epileptics (anticonvulsants) will be considered:

- carbamazepine (licensed for use in paroxysmal pain of trigeminal neuralgia only)
- oxcarbazepine (off-label use)
- gabapentin (licensed for use in peripheral neuropathic pain such as painful diabetic neuropathy and post-herpetic neuralgia only)
- pregabalin (licensed for use in central and peripheral neuropathic pain)
- phenytoin (licensed for use in trigeminal neuralgia only as second-line therapy if carbamazepine is ineffective or patients cannot tolerate carbamazepine)
- lacosamide (off-label use)
- lamotrigine (off-label use)

- levetiracetam (off-label use)
- sodium valproate (off-label use)
- topiramate (off-label use).

e) The following opioid analgesics will be considered:

(Please note that for this section, the summary product characteristics (SPC) varies according to the individual manufacturer end drug, please refer to the SPC for full details)

- paracetamol and opioid combinations:
 - co-codamol (licensed for mild, moderate, and severe pain)
 - co-dydramol (licensed for mild to moderate pain)
- morphine (licensed for chronic pain)
- dihydrocodeine (licensed for moderate to severe pain)
- oxycodone (licensed for severe pain, post-operative pain, and also moderate pain in patients with cancer)
- oxycodone with naloxone (licensed for severe pain which can be adequately managed only with opioid analgesics)
- tapentadol (licensed for moderate to severe acute pain or severe chronic pain in adults, which can be adequately managed only with opioid analgesics)
- tramadol (licensed for moderate to severe pain)
- buprenorphine (licensed for moderate to severe pain)
- fentanyl (licensed for severe pain or breakthrough cancer pain).

f) The following additional drugs will be considered:

- cannabis sativa extract (Sativex; off-label use, although it is licensed as an adjunct in moderate to severe spasticity in multiple sclerosis)
- flecainide (off-label use)
- 5-HT₁-receptor agonists (such as sumatriptan; off-label use for each of these)

- topical lidocaine (lidocaine medicated plaster, Versatis, is licensed for neuropathic pain associated with previous herpes zoster infection [post-herpetic neuralgia only])
- topical capsaicin (Axsain cream is licensed for the treatment of neuralgia associated with and following Herpes Zoster infections [post-herpetic neuralgia] and diabetic peripheral polyneuropathy only; Qutenza patch is licensed for peripheral neuropathic pain in non-diabetic adults only).

g) The above listed interventions will be compared with:

- placebo
- each other, if relevant evidence is available.

4.3.2 Clinical issues that will not be covered

- a) Diagnosis and assessment of neuropathic pain.
- b) Treatments other than those listed in 4.3.1 a–e.
- c) Treatment of the underlying causes of neuropathic pain and any associated disease-specific management.
- d) Acute post-surgical pain.
- e) Treatment of pain other than neuropathic pain.

4.4 Main outcomes

- a) Patient-reported global improvement, patient-reported pain relief, or both, measured on any standard subjective scales for pain intensity or pain relief (global improvement or pain relief of 30% or 50% or greater, or 50% or more reduction of the score on a validated pain scale).
- b) Patient-reported improvement in daily physical and emotional functioning, including sleep.

- c) Major adverse effects (defined as leading to withdrawal from treatment), and minor adverse effects (all adverse effects noted in patients' reports).
- d) Overall improvement in quality of life.
- e) Resource use and costs.

4.5 *Review questions*

- a) What is the clinical effectiveness of different pharmacological treatments as monotherapy compared with each other or placebo for the management of neuropathic pain in adults, outside of specialist pain management services?
- b) What is the clinical effectiveness of different pharmacological treatments as combination therapy compared with other combination therapies, monotherapy or placebo for the management of neuropathic pain in adults, outside of specialist pain management services?

4.6 *Economic aspects*

Developers will take into account both clinical and cost effectiveness when making recommendations involving a choice between alternative interventions. A review of the economic evidence will be conducted and analyses will be carried out as appropriate. The preferred unit of effectiveness is the quality-adjusted life year (QALY), and the costs considered will usually be only from an NHS and personal social services (PSS) perspective. Further detail on the methods can be found in 'The guidelines manual' (see 'Further information').

4.7 *Status*

4.7.1 *Scope*

This is the final version of the scope.

4.7.2 Timing

The development of the guideline recommendations will begin in July 2012.

5 Related NICE guidance

5.1 *Published guidance*

5.1.1 NICE guidance to be updated

This guideline will update and replace the following NICE guidance:

- [Neuropathic pain – pharmacological management](#). NICE clinical guideline 96 (2010).

5.1.2 Other related NICE guidance

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

5.2 *Guidance under development*

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

- Type 1 diabetes (update). NICE clinical guideline. Publication expected 2014.
- Type 2 diabetes (update). NICE clinical guideline. Publication expected 2014.

6 Further information

Information on the guideline development process is provided in the following documents, available from the NICE website:

- [How NICE clinical guidelines are developed: an overview for stakeholders the public and the NHS](#)
- [The guidelines manual](#).

Information on the progress of the guideline will also be available from the [NICE website](#).