NATIONAL INSTITUTE FOR HEALTH AND CLINICAL EXCELLENCE

SCOPE

1 Guideline title

Neuropathic pain: 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.'

3 Clinical need for the guideline

3.1 Epidemiology

a) Neuropathic pain refers to a heterogeneous group of disorders resulting from damage to, and dysfunction of, the peripheral and central nervous systems. Common examples of peripheral neuropathic pain include painful diabetic neuropathy, post-herpetic neuralgia and trigeminal neuralgia. Common examples of central neuropathic pain include 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 well-being 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 in specialist pain management clinics. However, there is limited evidence on the incidence and prevalence of neuropathic pain in non-specialist settings. 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.

a) 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 in non-specialist settings. These include antidepressants (tricyclic antidepressants – TCAs, and selective serotonin reuptake inhibitors – SSRIs) and antiepileptic 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 pains are 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). An ongoing systematic review of different treatment pathways for neuropathic pain, commissioned by the NIHR HTA programme, is due to be published in 2009 and should show which are the most clinically- and cost-effective strategies for the pharmacological management of neuropathic pain.

b) There is evidence that neuropathic pain is commonly managed in primary care and other non-specialist settings. However, there is considerable variation in practice in terms of how therapy is initiated, whether therapeutic doses are achieved 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 also ensure that only those people who need specialist assessment and interventions are referred on, which could reduce the volume of referrals to specialist pain management and neurology clinics.

c) There is currently no evidence-based guideline available in England, Wales and Northern Ireland that addresses the pharmacological management of overall neuropathic pain in adults in non-specialist settings.

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

b) Adults with neuropathic pain conditions managed in the settings described in section 4.2.

c) The guideline will give specific consideration to subgroups of older people with post-herpetic neuralgia or painful diabetic neuropathy.

4.1.2 Groups that will not be covered

a) Adults with neuropathic pain conditions that are managed in specialist pain management clinics.

b) Adults with neuropathic pain arising directly from trauma or orthopaedic surgical procedures.

4.2 Healthcare setting

a) Primary and secondary care, excluding specialist pain management clinics.

4.3 Clinical management

4.3.1 Key clinical issues that will be covered

a) The following antidepressants will be considered.

- Tricyclic antidepressants (TCAs):
  - amitriptyline (unlicensed indication)
  - clomipramine (unlicensed indication)
  - desipramine
  - dosulepin (unlicensed indication)
  - doxepin (unlicensed indication)
  - imipramine (unlicensed indication)
  - lofepramine (unlicensed indication)
  - nortriptyline (unlicensed indication)
  - trimipramine (unlicensed indication).

- Selective serotonin reuptake inhibitors (SSRIs):
  - citalopram (unlicensed indication)
  - fluoxetine (unlicensed indication)
  - paroxetine (unlicensed indication)
  - sertraline (unlicensed indication).
- Other antidepressant drugs (SNRIs):
  - duloxetine (licensed for diabetic peripheral neuropathy only)
  - venlafaxine (unlicensed indication).

b) The following antiepileptics (anticonvulsants) will be considered:

- carbamazepine (licensed for use in trigeminal neuralgia only)
- oxcarbazepine (unlicensed indication)
- gabapentin (licensed for use in peripheral neuropathic pain)
- pregabalin (licensed for use in central and peripheral neuropathic pain)
- phenytoin (licensed for use as second line therapy in trigeminal neuralgia if carbamazepine is ineffective or patients are intolerant to carbamazepine)
- lamotrigine (unlicensed indication)
- sodium valproate (unlicensed indication)
- topiramate (unlicensed indication).

c) The following opioid analgesics will be considered:

- paracetamol and opioid combinations:
  - co-codamol (licensed for mild to moderate pain)
  - co-dydramol (licensed for mild to moderate pain)
- morphine (licensed for moderate to severe pain)
- dihydrocodeine (licensed for moderate to severe pain)
- oxycodone (licensed for moderate to severe pain)
- tramadol (opioid effect and an enhancement of serotonergic and adrenergic pathways − licensed for moderate to severe pain)
- buprenorphine (licensed for moderate to severe pain)

- fentanyl (licensed for moderate to severe pain).

d) The following topical preparations will be considered:

- topical lidocaine (lidocaine medicated plaster, Versatis, is indicated for the symptomatic relief of neuropathic pain associated with previous herpes zoster infection [post-herpetic neuralgia])
- topical capsaicin (Axsain is licensed for the treatment of post-herpetic neuralgia and painful diabetic neuropathy).

e) The use of the drug therapeutic classes detailed in 4.3.1 a–d in non-specialist settings to manage neuropathic pain. These interventions will be compared with:

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

f) Use of the drug therapeutic classes detailed in 4.3.1 a–d, and their positioning within the care pathway for the management of neuropathic pain in non-specialist settings. This will include use of individual drugs as monotherapy and/or in combination, if clearly supported by evidence.

g) 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. This is indicated in the text. Note that guideline recommendations will normally fall within licensed indications; use outside a licensed indication may be recommended, but only if clearly supported by evidence of clinical effectiveness. The guideline will assume that prescribers will use a drug's summary of product characteristics to inform their decisions for individual patients.

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–d.

c) Treatment of the underlying causes of neuropathic pain and any associated disease-specific management.

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 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 costs will usually only be from an NHS and personal social services (PSS) perspective. Further detail on the methods can be found in 'The guidelines manual' (see section 6, 'Further information').

4.6 Status

4.6.1 Scope

This is the final scope.

4.6.2 Timing

The development of the guideline recommendations will begin in May 2009.

5 Related NICE guidance

5.1 Published guidance

- Type 2 diabetes (update). NICE clinical guideline 66 (2008). Available from www.nice.org.uk/CG66
- Type 1 diabetes. NICE clinical guideline 15 (2004). Available from www.nice.org.uk/CG15
- Multiple sclerosis. NICE clinical guideline 8 (2003). Available from www.nice.org.uk/CG8

5.2 Guidance under development

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

- Low back pain. NICE clinical guideline. Publication expected May 2009.

6 Further information

Information on the guideline development process is provided in:

- 'How NICE clinical guidelines are developed: an overview for stakeholders' the public and the NHS'
- 'The guidelines manual'.

These are available from the NICE website (www.nice.org.uk/guidelinesmanual). Information on the progress of the guideline will also be available from the NICE website (www.nice.org.uk).