Module 1917 Neuropathic pain: how to recognise and manage

From this pharmacy CPD module you will learn about:

- The causes, risk factors and symptoms of neuropathic pain
- How the condition is diagnosed and managed, including nonpharmacological options
- Self-care advice that pharmacists and their teams can offer to patients

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Neuropathic pain is a type of chronic pain that results from damage to the nerves. It can present as sensory (numbness, increased sensitivity), motor (weakness) and autonomic (temperature, sweating) changes.⁽¹⁾ It is defined as pain caused by a lesion or disease of the somatosensory nervous system⁽²⁾ – the part of the sensory system involved with the conscious perception of touch, pain, temperature, pressure, position and movement, which comes from the muscles, joints and skin.⁽³⁾

Neuropathic pain can be classified as peripheral or central, depending on whether it is the central or peripheral somatosensory nervous system that is affected.⁽²⁾

Causes of neuropathic pain

Possible causes of peripheral neuropathic pain include:

- excessive alcohol consumption
- vitamin B12 deficiency⁽¹⁾
- nerve damage after surgery or trauma
- nerve entrapment
- trigeminal neuralgia (a specific form of facial pain)
- postherpetic neuralgia (persistent pain after a shingles episode)
- diabetes resulting in painful diabetic

neuropathy

- infection from HIV or polio⁽¹⁾
- cancer from the tumour or treatment.⁽⁴⁻⁶⁾
 Possible causes of central neuropathic pain
 include:
- spinal cord injury
- stroke
- multiple sclerosis
- other neurological or metabolic conditions.^(5,6)

Risk factors for neuropathic pain

There are a range of factors that can increase a patient's risk of developing neuropathic pain, including:

- increasing age
- female gender
- sedentary lifestyle
- physically demanding occupations
- genetic factors.⁽⁷⁾

Factors that predispose people to developing conditions that may put them at increased risk of peripheral neuropathy should also be considered, as well as factors that help to decrease the chance of developing neuropathic pain once a person is diagnosed with a condition.

Diabetes, for example, can increase the risk of painful diabetic neuropathy. Consuming a healthy diet and increasing exercise may help to mitigate the development of diabetes. However, if someone already has diabetes, tight control of blood sugar levels, by diet and pharmacological management, will help to decrease the risk.⁽⁷⁾

How common is neuropathic pain?

Estimates of overall incidence and prevalence of neuropathic pain vary; prevalence is estimated to be between 6% and 8%. This is higher when looking at specific conditions – 16-26% of diabetic patients have painful diabetic neuropathy and 8-19% of patients with herpes zoster suffer from post-herpetic neuralgia (defined as pain at one month after rash onset).⁽⁵⁾

Neuropathic pain symptoms

As the name suggests, the main symptom is pain. However, neuropathic pain is usually described by people as pain that is shooting, stabbing or burning in nature and is very unpleasant; it can present as constant or intermittent, and be spontaneous or triggered.⁽⁵⁾ It can also be described as pain that is tingling, numb, itching, prickly, like an electric shock, pins and needles, tight or an altered sensation.^(5,6,8)

Some patients find the condition hard to describe: "I began to feel disconnected from my feet, but could not describe that feeling to my doctor."^(6,9) Symptoms of allodynia (pain caused by a stimulus that does not normally cause pain), anaesthesia dolorosa (pain felt in a numb area or region), hyperalgesia (increased response to something that is normally painful) or sensory gain or loss may present.⁽⁵⁾

Other pain that may be non-neuropathic (eg osteoporosis or cancer pain) may have neuropathic characteristics.⁽⁶⁾

People who present to the pharmacy with



Neuropathic pain is defined as pain caused by a lesion or disease of the somatosensory nervous system



Nice recommends antidepressants and antiepileptics (eg pregabalin), as first-line treatment in neuropathic pain

symptoms suggestive of neuropathic pain and have not seen a doctor should be referred. They will need to be assessed for possible underlying causes, accurate diagnosis and, if applicable, given appropriate treatment.

How is it diagnosed?

Diagnosis is based on physical examination and patient history,⁽¹⁰⁾ and involves finding evidence of a nerve lesion, pain in response to light touch, or reduced or increased sensitivity and altered sensation.⁽⁶⁾ Questionnaires have been developed that are based on sensory descriptors and sensory examination and help clinicians to differentiate between pain that is of a somatic origin or neuropathic origin.

The Leeds Assessment of Neuropathic Symptoms and Signs (LANSS) is an assessment tool completed at the bedside in two parts and is accepted as a valid way to help differentiate between neuropathic and nociceptive pain (pain caused by a stimuli).⁽¹¹⁾ Certain blood tests may also be ordered or nerve conduction studies performed; the latter involves using needles to test the flow of small electric currents through the nerves.⁽¹⁾

Prognosis

Neuropathic pain tends to be persistent. This is because, in many cases, the causes are complex and diverse and it is usually not possible to cure the underlying disease or lesion.⁽⁷⁾ The pain tends to be more severe and is associated with poorer physical and mental health, when compared with chronic pain of non-neuropathic origin.^(7,8) One UK study found that 17% of people with neuropathic pain had health-related quality of life scores equivalent to "worse than death".⁽⁷⁾ The response to drug treatment tends to be inadequate,⁽⁸⁾ and many cases remain undertreated or untreated,⁽⁷⁾ despite the availability of many effective drugs and guidelines around the world.⁽⁶⁾ In order to reduce the incidence and impact of neuropathic pain, healthcare professionals need to address the risk factors and ensure patients are given treatments with known effectiveness.⁽⁷⁾

Management

The management of neuropathic pain involves pharmacological and non-pharmacological treatments. Guidelines around the world differ slightly in their recommendations; however, most tend to be in agreement about first- and second-line recommendations: antiepileptics or antidepressants.

The use of opioids in the treatment of neuropathic pain remains contentious, as there is no strong evidence supporting their use.⁽¹⁰⁾ The limitations to opioid treatment include:

- side effect profiles
- patients not achieving satisfactory pain relief intolerance.

Over-the-counter analgesics, such as paracetamol, non-steroidal anti-inflammatory drugs (NSAIDs), and weak opioid drugs (eg codeine) are not usually effective for neuropathic pain.⁽¹⁾

The National Institute for health and Care Excellence (Nice) recommends the antidepressants amitriptyline and duloxetine, or the antiepileptics gabapentin and pregabalin, as first-line treatment options for people with all types of neuropathic pain, except trigeminal neuralgia.⁽⁵⁾ Venlafaxine, nortriptyline and desipramine are recommended as first-line treatment options in some other countries.⁽¹⁰⁾

Nice recommends tramadol only for acute rescue therapy in short courses. $^{\scriptscriptstyle (5,8)}$

There is increasing evidence from different countries of the efficacy of cannabis-based products to treat different types of pain. In November 2018, the UK moved "cannabisderived medicinal products of the appropriate standard" from schedule 1 to schedule 2 controlled drugs. This means cannabis-based products (excluding synthetic cannabinoids) can be prescribed medicinally where there is an unmet clinical need.

Due to the limited evidence base and their unlicensed nature, the government has chosen to restrict the decision to prescribe cannabisbased products for medicinal use to only those clinicians listed on the General Medical Council's specialist register. As with any unlicensed medicines or "specials", the prescribing of such products must be on a "named patient" basis.

NHS England expects that cannabis-based products for medicinal use should only be prescribed for indications where there is clear published evidence or UK guidelines, and for patients with a clinical need which cannot be met by a licensed medicine and for whom established treatment options have been exhausted.

Other options include selective serotonin reuptake inhibitors (SSRIs) – such as citalopram, paroxetine and escitalopram – lamotrigine, lacosamide, methadone and topical lidocaine. Tapentadol, capsaicin cream and botulinum toxin (eg Botox) may also be beneficial. Nice recommends using capsaicin 0.075% cream as an alternative for patients who have localised pain and when oral treatment is not tolerated or suitable.⁽⁵⁾

Combination pharmacotherapy may be prescribed to improve analgesic efficacy and possibly reduce side effects – typically the drugs used are synergistic and will allow for dose reductions.⁽¹²⁾ However, Nice guidelines do not recommend combination pharmacotherapy, instead recommending switching first-line drugs and ensuring an adequate trial period.⁽⁵⁾

A Cochrane review of combination pharmacotherapy found that gabapentin with an opioid produced a modest, yet superior, effect over gabapentin alone. However, there were significantly higher side effect-related dropouts. The difference in recommendations highlights the lack of evidence currently available to recommend any one particular combination over another. Interestingly, multiple studies show superior efficacy of two-drug combinations, therefore providing a rationale for combination therapy.⁽¹²⁾

First-line drugs recommended by Nice can be started in primary and secondary care, but referral to specialist care should occur if:

- there is severe pain
- the pain is significantly limiting daily activities and lifestyle
- the underlying health condition has deteriorated.

Specialists may prescribe cannabis sativa extract, capsaicin patch, lacosamide, lamotrigine, levetiracetam, morphine, oxcarbazepine, topiramate, tramadol for long-term use, venlafaxine or sodium valproate.⁽⁵⁾

Nice recommended therapies

The drugs recommended by Nice for the treatment of neuropathic pain may or may not be licensed. Prescribers should follow relevant professional guidance and will take full responsibility for their prescribing decisions.⁽⁵⁾

Amitriptyline

This tricyclic antidepressant's pain-reducing effect is independent of the mood-altering properties of the drug, but the mechanism of its action in managing pain is not fully understood. It is licensed for neuropathic pain in adults and has a starting dose of 10mg at night.⁽¹⁶⁾ This can be titrated up to a maximum of 75mg a day (above 75mg only on specialist advice).⁽⁸⁾ Its analgesic effect is typically seen after two to four weeks of use.⁽¹⁶⁾

Patients should be trialled for six to eight weeks, with two weeks at maximum dose before deciding it is ineffective. If amitriptyline is discontinued, this should be done gradually over four weeks to prevent discontinuation symptoms.⁽⁸⁾ Side effects include dry mouth, sleepiness, dizziness and constipation.⁽¹⁶⁾

Pregabalin

This binds to presynaptic voltage-gated channels in the dorsal horn, reducing the release of excitatory neurotransmitters, such as glutamate and substance P.⁽²⁵⁾ It is licensed for diabetic peripheral neuropathic pain in adults⁽¹⁸⁾ and is given as 150mg per day (given in two to three divided doses).^(8,17) This can be titrated to 300mg per day after three to seven days, and may be increased to a maximum dose of 600mg per day after a further seven days.^(8,17)

Side effects include dizziness, somnolence, increased appetite and weight gain.⁽⁸⁾ You should be aware that lower doses may be necessary in patients with reduced renal function⁽⁸⁾ and, if the medicine is discontinued, this should be done so gradually over at least one week.^(8,17)

Gabapentin

As with pregabalin, this medicine binds to presynaptic voltage-gated channels in the dorsal horn of the spinal cord, reducing the release of excitatory neurotransmitters, such as glutamate and substance P.⁽²⁵⁾ Gabapentin is licensed for peripheral neuropathic pain, such as painful diabetic neuropathy and post-herpetic neuralgia in adults.⁽¹⁹⁾

The starting dose of gabapentin is dependent on the patient and can be between 100-300mg daily. This dose can be increased every few days depending on the patient's response, up to a maximum dose of 3,600mg per day in three divided doses. The onset of action is two weeks, with a peak effect usually after eight weeks at therapeutic doses. It is usually trialled for three to eight weeks (at least two weeks at maximum tolerated dose) before deciding if it is ineffective and discontinuing therapy if necessary. When the medicine is discontinued, it should be done so gradually over a period of at least one week. Gabapentin side effects may include dizziness, drowsiness, increased appetite and weight gain.⁽⁸⁾

Duloxetine

This serotonin and noradrenaline reuptake inhibitor has been shown to normalise pain



Some patients may benefit from non-pharmacological treatments, such as physiotherapy

thresholds.⁽¹⁸⁾ The inhibitory effect on pain is believed to be due to potentiation of descending inhibitory pain pathways contained in the central nervous system. It is licensed for diabetic peripheral neuropathic pain in adults and has a starting dose of 60mg per day. This can be increased, if necessary, to 120mg per day in divided doses.^(8,18)

You should make patients starting this medicine aware that it may take some time for the medicine to have an effect. Patients should be trialled for up to eight weeks before deciding whether the treatment is ineffective, and the dose should be reassessed every three months. If this medicine requires discontinuation, this should be done gradually over at least one to two weeks to reduce discontinuation symptoms.^(B) Side effects of duloxetine include nausea, sleepiness, dizziness, decreased appetite and constipation.

Capsaicin

Capsaicin 0.075% w/w cream is thought to deplete and prevent reaccumulation of substance P in peripheral sensory neurons, thereby rendering the skin insensitive to pain. It is licensed for painful diabetic neuropathy (under supervision of a hospital consultant) and postherpetic neuralgia (after open lesions have healed).⁽²⁰⁾

A small amount of the cream (pea size) should be applied to the affected area three to four times per day.^(8,20) Onset of effect usually occurs after one week; however, the effect increases with regular application over the following two to eight weeks.⁽⁸⁾ Advise patients not to apply to broken or irritated skin. Side effects, such as skin irritation and a burning sensation, may limit use.⁽⁸⁾ Advise patients to avoid inhalation of vapours produced by the capsaicin and not to have hot baths or showers immediately before or after treatment.⁽²⁰⁾

Non-pharmacological treatments

These involve pain management techniques,

physiotherapy, psychological therapies and some more invasive interventions. Pain management techniques include massage therapy, relaxation and music, while exercises involving aerobics, flexibility, strength and balance may reduce neuropathic pain when performed regularly.⁽¹³⁾ A chronic pain physiotherapist will be able to give advice about how to exercise without aggravating pain.⁽¹⁾

Psychological and cognitive behavioural therapy (CBT) have shown some benefits in the treatment of chronic pain.⁽⁴⁾ Some more invasive non-pharmacological treatments for use in specialist settings include spinal cord stimulation, percutaneous electrical nerve stimulation and deep brain stimulation.

Other non-pharmacological measures, such as acupuncture, homeopathy, or transcutaneous electrical nerve stimulation (TENS), do not have sufficient evidence to support their use.⁽⁴⁾

Self-care

Many people go to pharmacies around the UK every day to purchase painkillers, therefore pharmacists and pharmacy staff are ideally placed to screen patients who may be suffering from pain to ensure it is not neuropathic and help increase awareness.

Neuropathic pain can easily be overlooked and treated as musculoskeletal pain, which may result in inappropriate treatment and months or years of mismanagement.

You should ensure when speaking to patients that you review all components of pain: onset and duration; location; severity; if anything makes the pain worse or helps the pain to subside; and any emotional factors that may be playing a role.

Ensure you are listening out for any key words

Neuropathic pain CPD - planned learning

What are you planning to learn?

I want to learn more about the causes, risk factors and symptoms of neuropathic pain, as well as pharmacological and non-pharmacological treatment options. I also want to improve my knowledge of the self-care advice that pharmacists and their teams can offer to patients suffering from neuropathic pain.

This learning will help me to improve my knowledge of neuropathic pain and to be able to confidently provide advice to patients and carers, to spot at-risk patients and know when to refer.

How are you planning to learn it?

- I plan to find out more about neuropathic pain on the Patient website at tinyurl.com/neuropathicpain1.
- I plan to improve my knowledge of how exercise can help those with neuropathic pain on the Foundation for Peripheral Neuropathy website at *tinyurl.com/neuropathicpain2*.
- I plan to read about how adopting a positive mental attitude can help those with neuropathic pain on the Foundation for Peripheral Neuropathy website at *tinyurl.com/neuropathicpain3*.

Give an example of how this learning has benefited the people using your services

I carried out an MUR with a middle-aged diabetic male patient who seemed to be much more withdrawn than usual. He had no side effects from his medication and was well informed about his condition. However, he did ask for advice about painkillers for a burning pain in his legs and feet, which was making it difficult for him to walk at times and was not relieved by paracetamol. I asked him further questions to find out more about his pain, explained that it may be linked to his diabetes and referred him to his GP.

that may indicate neuropathic pain – 'burning', 'tingling', 'stabbing' are usually specific to neuropathic pain – or for references to the patient finding sleeping under the bed sheets painful (allodynia). It is a good idea to ask all patients who request painkillers to describe their pain. Patients with neuropathic pain usually have a long history of seeking treatment, as the relief they get is only partial, which may be due to misdiagnosis or inappropriate medication.⁽¹⁴⁾

For patients with a diagnosis of neuropathic pain, you can offer advice about keeping active. Some patients may find that a hot or cold pad on the area will help, but you should check with the patient's primary care physician before recommending this technique.⁽¹⁵⁾ Patients with neuropathic pain often have comorbidities, such as insomnia, anxiety and depression.⁽¹⁴⁾ Appropriate questioning should be employed to assess for these conditions and refer where necessary.

Further information for patients and carers

Pain Concern is a charity that works to support and inform people with pain and those who care for them. It has a patient information booklet on neuropathic pain, which is downloadable and can be printed and given to patients, at *painconcern.org.uk/neuropathic-pain*.

The Foundation for Peripheral Neuropathy (*foundationforpn.org*) is a public charity foundation based in the USA. Its website contains

References for this module can be found online by visiting *bit.ly/UPDATE-PLUS* and searching: 1917

Take the 5-minute test online

- Neuropathic pain is chronic pain resulting from nerve damage and can present as sensory, motor and autonomic changes. True or false
- 2. Risk factors for neuropathic pain include increasing age, female gender, sedentary lifestyle and physically demanding occupations.

True or false

- An estimated 30-40% of diabetic patients suffer from painful diabetic neuropathy. True or false
- Allodynia is where pain is felt in a numb area or region.
 True or false
- Neuropathic pain tends to be more severe and is associated with poorer physical and mental health when compared with chronic pain of non-neuropathic origin.
 True or false

- Simple analgesics, such as paracetamol and NSAIDs, and weak opioid drugs, such as codeine, do not usually work for neuropathic pain.
 True or false
- Nice guidelines recommend combination analgesic pharmacotherapy for first-line management of neuropathic pain.
 True or false
- Amitriptyline's mode of action in pain management is well understood. True or false
- Side effects of duloxetine include nausea, sleepiness, dizziness, decreased appetite and constipation.
 True or false
- For the management of neuropathic pain, capsaicin cream should be applied to the affected area once daily.
 True or false

You can complete the quiz and logsheet by visiting *bit.ly/UPDATE-PLUS* and searching: 1917