Neuropathic Pain in Adults- Guideline for Primary Care

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Document Control

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Revision history

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Approvals

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Contents

FOREWORD

Neuropathic pain is managed in many patients by the use of simple scales to measure the pain itself, a review of both physical and psychological functional impairment, and pharmacological and non-pharmacological treatments coupled with an idea of the patient's goals/expectations for the management of the pain. Some patients who suffer from pain that does not respond to standard therapies may require a more in-depth assessment and will need to be referred to secondary care.

One of the aims of this document is to aid with differentiating those patients who can be managed very successfully in primary care and those who require involvement of healthcare professionals in secondary care. Many patients who are already within a secondary care setting but go on to develop neuropathic pain (whilst under another speciality e.g., orthopaedics) are often referred directly to pain clinics when they can be managed quite effectively by primary care in the first instance.

This document has been developed utilising the latest clinical evidence. It has been adapted to include treatments based on clinical experience whilst also considering the best use of scarce NHS resources for the whole GM population.

Whilst this guideline is primarily for primary care, we would expect the same principles to apply in a secondary care setting.

GMMMG

AIM

To promote the rational use of pharmacotherapies, and associated adjuvant treatment, so that neuropathic pain is optimally managed.

Implementation of the guidance aims to improve the safe and effective use of treatments for the symptomatic relief of neuropathic pain.

This guideline is based on the *Neuropathic pain in adults: pharmacological management in non-specialist settings, NICE CG 173,* (updated September 2020) with some local adaptation.

1. Introduction

1.1 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'.

1.2 Neuropathic pain is very challenging to manage because of the heterogeneity of its aetiologies, symptoms, and underlying mechanisms. 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.

1.3 Examples of common conditions that have peripheral neuropathic pain as a symptom are painful diabetic neuropathy, post-herpetic neuralgia, trigeminal neuralgia, 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.

1.4 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, and itching and a sensation of pins and needles.

1.5 The prevalence of neuropathic pain is difficult to quantify and varies depending on the cause of pain. For example, it may affect up to a quarter of people with diabetes, and 10-50% of people who have received surgery. The experience of pain is always influenced by social factors (including deprivation, isolation, lack of access to services), emotional factors (including anxiety, distress, previous trauma), expectations and beliefs, mental health (including depression and post-traumatic stress disorder) and biological factors. All these potential contributors should be considered during neuropathic pain assessment. It is crucial to set realistic expectations and treatment goals. Achieving pain free status is not always possible. **Reduction in pain by 50% is a commonly used endpoint in clinical trials.** See information for patients section for example leaflets that are available that could be used to aid these discussions.

1.6 Screening tools can be useful to aid diagnosis: the Neuropathic Pain Scale (NPS) is a well-known validated scale (see **appendix 1**). Evidence supports the validity of the NPS for detecting change in pain after treatments; however other pain scales are available.

1.7 **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.**

2. Key principles of care

2.1 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.
- 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.
- Setting realistic expectations of treatment. Achieving pain free status may not be achievable. Response to drug treatment is often inadequate, with no more than 40-60% of people obtaining partial pain relief.
- 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).**

2.2 Consider referring the person to a specialist pain service and/or a condition specific service at any stage, including at initial presentation and at the regular clinical reviews if:

- No significant improvement after a suitable trial period (see relevant drug sections below), or
- Their underlying health condition has deteriorated, or
- They have severe pain, or
- Their pain significantly limits their lifestyle, daily activities (including sleep disturbance) and participation.

It is important that patients' expectations are realistic when considering the management of pain. Achieving pain free status is not always possible, <u>despite</u> referral to the pain clinic.

2.3 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
- physical and psychological wellbeing
- adverse effects
- continued need for treatment

2.4 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.

2.5 All treatments should be titrated appropriately and given for an adequate duration prior to moving to the next option.

3. Algorithm for management of neuropathic pain (for trigeminal neuralgia see section 4.3)

1st line:

Amitriptyline: 10-75mg for 6-8 weeks (usual max 75mg)

- Doses >75mg and ≤100mg can be used cautiously in consultation with a specialist pain service if the patient is deriving benefit with limited side effects.
- If amitriptyline is effective but too sedative offer nortriptyline (10-75mg for 6-8 weeks).

- **Amitriptyline** is licensed for neuropathic pain in adults
- For suggested dose titration and adjustment see 4.2.1
- Titrate slowly to reduce side effects; this also applies to dose reduction/ discontinuation
- Best taken in the evening to reduce hangover effect e.g., 6-8pm
- ***For advice on driving or operating machinery, see 4.1 and drug SPC***
- For nortriptyline further info see 4.2.1

Continue if pain is well controlled. Consider gradual dose reduction if improvement is sustained.

If treatment is ineffective, **discontinue gradually** and consider:

2nd line:

Gabapentin: 1200mg-3600mg/day in three divided doses for 3-8 weeks.

- An adequate trial should include at least 2 weeks at the **maximum tolerated** dose before deciding gabapentin is ineffective.

- Consider switching to pregabalin: 150mg to 600mg/day for 4 weeks if intolerable side-effects occur.
- Advice on switching can be found here.

- **Gabapentin** is licensed for peripheral neuropathic pain (diabetic neuropathy/ post-herpetic neuralgia)
- For suggested dose titration and adjustment see 4.2.2
- ***For advice on driving or operating machinery, see 4.1 and drug SPC***
- **Pregabalin** is licensed for peripheral and central neuropathic pain
- For suggested dose titration and adjustment see 4.2.3
- ***For advice on driving or operating machinery, see 4.1 or drug SPC***
- **Pregabalin** and **gabapentin** are controlled drugs. Prescription requirements apply, see 4.2.7. A maximum of 30 days treatment should be prescribed at a time

Continue if pain is well controlled. Consider gradual dose reduction if improvement is sustained.

If treatment is ineffective, **discontinue gradually** and consider:

3rd line:

Duloxetine: 60mg-120mg/day titrated slowly.

- **Duloxetine** may be considered **1st line** for patients with a clear diagnosis of diabetic neuropathy.
- **Duloxetine** may also be an option in patients with a history of substance misuse, particularly in a prison setting.

- **Duloxetine** is licensed for diabetic peripheral neuropathic pain
- For suggested dose titration and adjustment see 4.2.4
- Treatment should be assessed at least every three months
- ***For advice on driving or operating machinery, see 4.1 or drug SPC***

Non-oral options:

Capsaicin 0.075% cream: as per NICE CG173 may be considered for localised neuropathic pain in patients who wish to avoid or cannot tolerate oral options. This treatment is 'off label'.

- Apply a pea-sized amount 3-4 times a day (no more often than every 4 hours) to the affected area (max 8 weeks). It is recommended the patient is re-assessed prior to continuation beyond 8 weeks.

Consider referral to specialist pain services/ condition specific services if any of the following:

- pain is severe
- pain significantly limits lifestyle, daily activities (including sleep disturbance) and participation
- deterioration of underlying health condition(s)

Tramadol should only be considered for short-term as rescue therapy in patients awaiting referral to specialist pain services, where initial treatments have failed.

LONG TERM USE IS NOT RECOMMENDED.

4. Pharmacological treatment

Please note that this information is a summary to guide prescribers – for further information please consult individual SPCs at www.medicines.org.uk

4.1 Effects on ability to drive and use machines

- Pharmacological treatment options for neuropathic pain are associated with sedative properties; particularly amitriptyline, gabapentin and pregabalin for which dizziness and somnolence are the most commonly reported side effects.
- **Patients should be advised not to drive, operate heavy machinery, or engage in other potentially hazardous activities until it is known whether the medication affects their ability to perform these activities**.
- If patients are prescribed tramadol, then they should be appropriately cautioned on the legality of driving as per DVLA legislation.

4.2 Neuropathic pain (except trigeminal neuralgia (see 4.3) and sciatica (see 4.4))

- Some products are not specifically licensed for all types of neuropathic pain and it is important to advise patients of this. Information and advice on prescribers' responsibilities when prescribing off - label medicines can be found here.

- **Due to a lack of evidence for the safety and cost-effectiveness of combining treatments, do not prescribe more than one neuropathic pain drug at the same time, unless on the advice of an NHS pain specialist.** For example, do not prescribe amitriptyline concurrently with duloxetine, gabapentin, or pregabalin.

- Avoid use of multiple serotonergic drugs where possible due to increased risk of serotonin syndrome (e.g., for neuropathic pain and depression) and assess patients holistically to minimise the number of medicines prescribed where possible (calculate anticholinergic burden). For further information please see SPS serotonin syndrome and ACB calculator.

- If pain is well controlled, continue treatment. Consider gradually reducing the dose over time if the improvement is sustained.

4.2.1 Offer amitriptyline first line

- Analgesic effect of amitriptyline is separate from its antidepressant effect.
- Amitriptyline is licensed for neuropathic pain in adults.
- It is best taken in the evening to reduce 'hangover effect' e.g., 6-8pm.
- Titrate slowly to reduce side-effects. Slow titration should also apply to dose reduction/ discontinuation.

- **Typical titration**:
  - Initially 10 to 25 mg daily, dose to be taken in the evening, then it can be increased, if tolerated, in steps of 10 to 25 mg every 3–7 days in 1–2 divided doses.
  - Usual dose is 25 to 75 mg daily

- The usual maximum dose is 75mg daily but up to 100mg can be used with caution, and on specialist advice, if the patient is deriving benefit with limited side-effects.
- The dose can be taken once daily or be divided into two doses. A single dose above 75mg is not recommended.
- Doses higher than 75mg should only be considered in consultation with a specialist pain service and should be used with caution in the elderly (increased risk of side effects, e.g., sedation and confusion) and in patients with cardiovascular disease.
- Caution on concurrent use of amitriptyline with other antidepressants or serotonergic opiates (e.g., fentanyl, oxycodone, tapentadol, tramadol). Consider trialling amitriptyline for 6-8 weeks, with at least 2 weeks at the maximum dose before deciding it is not effective. Clinical judgement

should be used to decide whether to titrate the dose more slowly upwards instead of switching (especially if adverse effects improve with time following each dose increase)
- If amitriptyline is not tolerated it should be withdrawn gradually over a minimum of 4 weeks to prevent discontinuation symptoms (such as dizziness, nausea, paraesthesia, anxiety, diarrhoea, flu-like symptoms, and headaches). There is no typical reducing regimen for amitriptyline; approach to down-titration will depend on patient specific factors including severity of pain, duration of therapy, magnitude of dose, incidence of adverse effects or discontinuation symptoms.
- There is no convincing evidence for the effectiveness of nortriptyline in neuropathic pain. However, as it is advocated by some sources as a substitute where amitriptyline is effective but too sedating, if prescribed, use only 10mg and 25mg tablets as these are the most cost effective.
- Nortriptyline should be used initially as 10mg once daily (at night) and increased gradually up to 75mg if necessary. Higher dose should be given under specialist supervision.

4.2.2 Offer gabapentin second line

- If the maximum dose of amitriptyline is unsuccessful in controlling pain or amitriptyline is not tolerated or not suitable, then the patient should be switched to gabapentin, titrating the dose gradually to prevent adverse effects, until effective pain relief is achieved.
- Gabapentin is licensed for the treatment of peripheral neuropathic pain in adults such as diabetic neuropathy and post herpetic neuralgia. Use for other conditions is off-label. Information and advice on prescribers' responsibilities when prescribing off-label medicines can be found here.
- Gabapentin has been associated with a rare risk of severe respiratory depression, even in patients not receiving concomitant opioid medicines. Caution is advised in patients at risk of respiratory depression.
- Various dose titrations may be used for gabapentin, depending on the person taking it and how well they tolerate it. The speed of titration will vary among individuals and should be tailored to the individual; if the person is elderly or frail they are more likely to experience adverse effects and will require slower titration. The dose should be adjusted for renal impairment (see table below). See examples of suggested approaches below.

Fast titration (usually suitable for otherwise healthy younger adults):

- Start with 300 mg once a day on day 1, then 300 mg twice a day on day 2, then 300 mg three times a day on day 3.
- Alternatively, start with 300 mg three times a day on day 1, then increased according to response in steps of 300 mg (in 3 divided doses) every 2–3 days up to maximum of 3600 mg a day (1200 mg three times a day).
- If the person experiences adverse effects during daily titration, a slower titration may help, or a lower maximum dose may be appropriate.

Slow titration (suitable if the person is elderly, frail, or has experienced adverse effects with higher doses):

- Start with 100 mg at night, increasing by 100 mg a day until pain is significantly reduced, intolerable adverse effects occur, or a maximum daily dosage of 3600 mg (1200 mg three times a day) is reached.
- If the person experiences adverse effects during daily titration, a slower titration (for example increasing the dose every 3–7 days) may help or a lower maximum dose may be appropriate.

Renal impairment (recommended dose adjustment as per BNF and CKS)**:**

Renal function eGFR (mL/min/1.73m^2)	Maximum starting daily dose	Maximum daily dosage
50-79	200mg TDS	600mg TDS
30-49	100mg TDS	300mg TDS
15-29 (stage 4, severe impairment)	100mg TDS on alternate days	200mg TDS

<15 (stage 5, very severe or end stage)	100mg TDS on alternate days	100mg TDS

- It may take several weeks to reach an effective dosage (usually 1200 mg to 3600 mg daily). Onset of action may be seen as early as the second week of treatment with rapid titration, but the peak effect usually occurs about 2 weeks after a therapeutic dosage is achieved (therefore an adequate trial may be 2 months or longer).
- Consider trialling gabapentin for 3–8 weeks, with at least 2 weeks at the maximum **tolerated** dose, before deciding it is not effective.
- Gabapentin should be discontinued gradually over a minimum of 1 week. **There is no typical reducing regimen for gabapentin; approach to down-titration will depend on patient specific factors including severity of pain, duration of therapy, magnitude of dose, incidence of adverse effects or discontinuation symptoms.**
- Discontinuation symptoms may include: anxiety, insomnia, nausea, pains, sweating.
- Controlled drug prescription requirements apply- see section 4.2.7.

4.2.3 Offer pregabalin if gabapentin is not tolerated

- Pregabalin may be considered in patients who cannot tolerate gabapentin, or who have not responded fully despite an adequate, fully documented trial. Advice on switching between gabapentin and pregabalin can be found here.
- Pregabalin is licensed for the treatment of peripheral and central neuropathic pain in adults. Use for other conditions is off-label. Information and advice on prescribers' responsibilities when prescribing off-label medicines can be found here.

Typical titration:

- Start pregabalin treatment at 150 mg a day (given in two to three divided doses).
- If necessary, increase the dose after 3 to 7 days to 300 mg a day (given in two to three divided doses).
- The dose can be increased further to a maximum dose of 600 mg a day (given in two to three divided doses) after an additional 7-day interval.
- A lower starting dose may be appropriate for some people, for example people who cannot initially tolerate 150 mg a day or people with reduced renal function (see below). A lower maximum dose may also be appropriate.

Renal impairment (recommended dose adjustment as per BNF and CKS)**:**

Renal function eGFR (mL/min/1.73m^2)	Maximum starting daily dose	Maximum daily dosage
30-60 (stage 3, moderate impairment)	75 mg a day (divided in two or three doses)	300 mg a day (divided in two or three doses)
15-29 (stage 4, severe impairment)	25–50 mg a day (as one daily dose or divided in two doses)	150 mg a day (as one daily dose or divided in two doses)
<15 (stage 5, very severe or end stage)	25 mg once a day	75 g once a day

- Consider trialling pregabalin for 4 weeks before deciding it is not effective.
- If pregabalin is not effective or tolerated, discontinue treatment gradually over a minimum of 1 week. **There is no typical reducing regimen for pregabalin; approach to down-titration will depend on patient specific factors including severity of pain, duration of therapy, magnitude of dose, incidence of adverse effects or discontinuation symptoms.**
- Discontinuation symptoms may include: insomnia, headache, nausea, anxiety, diarrhoea, flu syndrome, nervousness, depression, pain, convulsion, hyperhidrosis and dizziness suggestive

of physical dependence; incidence and severity may be dose related. The patient should be informed about this at the start of the treatment.
- Controlled drug prescription requirements apply- see section 4.2.7.

4.2.4 Offer duloxetine as third line, or first line for diabetic neuropathy

- Duloxetine may be considered as an option where other treatments have failed or for a clear diagnosis of diabetic neuropathy.
- Duloxetine is licensed for the treatment of diabetic peripheral neuropathic pain. Use for other conditions is off-label. Information and advice on prescribers' responsibilities when prescribing off-label medicines can be found here.

Typical titration:

- Start at 60 mg per day. A lower starting dose of 30mg may be appropriate for some people (for example, if tolerability is a problem).
- Titrate upward to an effective dose or the person's maximum tolerated dose of no higher than 120 mg per day (in two divided doses).
- Use only 30mg and 60mg capsules as these are the most cost effective.

Renal impairment (recommended dose adjustment as per BNF and CKS)**:**

- No dosage adjustment is necessary for people with mild or moderate renal impairment (eGFR ≥30mL/min/1.73m^2). At more advanced levels of renal impairment (eGFR<30ml/min/1.73m$^)$, elevated plasma concentrations occur and use should be avoided unless and only on specialist advice and providing the patient is closely monitored.

- Consider trialling duloxetine for up to 8 weeks before deciding it is not effective. Additional response after 8 weeks is unlikely.
- Treatment should be assessed at least every three months.
- If duloxetine is not effective or not tolerated, discontinue treatment gradually over a minimum of 1 to 2 weeks in order to reduce the risk of withdrawal reactions. **There is no typical reducing regimen for duloxetine; approach to down-titration will depend on patient specific factors including severity of pain, duration of therapy, magnitude of dose, incidence of adverse effects or discontinuation symptoms.**
- Discontinuation symptoms may include: dizziness, sensory disturbances (including paraesthesia or electric shock-like sensations, particularly in the head), sleep disturbances (including insomnia and intense dreams), fatigue, somnolence, agitation or anxiety, nausea and/or vomiting, tremor, headache, myalgia, irritability, diarrhoea, hyperhydrosis and vertigo.

4.2.5 Tramadol for acute rescue therapy

- Consider tramadol **only** if acute rescue therapy is needed
- Tramadol is licensed for the treatment of the treatment of moderate to severe pain but is not specifically licensed for neuropathic pain.
- The dose of tramadol is 50 to 100 mg not more often than every 4 hours (up to a maximum of 400 mg a day) titrated according to the pain severity.
- It should be reserved for people awaiting referral to specialist pain services, after initial treatments have failed. However, if there is a long waiting time to be seen by specialist this treatment may not be appropriate. Tramadol should be prescribed as a short course, cautiously, and bearing in mind the potential for misuse. Patients should be appropriately cautioned on the legality of driving while taking tramadol, as per DVLA legislation. Controlled drug prescription requirements apply- see section 4.2.7.

Prescribers are reminded that tramadol is a schedule 3 CD due to increases in the numbers of deaths relating to its misuse over the last few years. ***TRAMADOL IS NOT RECOMMENDED FOR LONG TERM USE.***

4.2.6 Non-oral options

- For patients with localised neuropathic pain who wish to avoid, or cannot tolerate oral treatments, consider prescribing capsaicin cream 0.075%; a pea-sized amount to be applied to the affected area 3 or 4 times daily (not more often than every 4 hours) for a maximum of 8 weeks. After this time, it is recommended that the patient's condition should be re-assessed before continuation of therapy. There are no efficacy data available to support treatment beyond 8 weeks.

- Lidocaine medicated plasters (700mg equivalent to 5%) are only licensed for use for post-herpetic neuralgia. They are listed as a GREY/GREEN drug by GMMMG; only to be used in patients who have been treated in line with NICE CG173 but are still experiencing neuropathic pain associated with previous herpes zoster infection (post-herpetic neuralgia). Use of lidocaine medicated plasters for indications other than post-herpetic neuralgia is not supported by GMMMG, or by NHSE in their Guidance for CCGs on Items which should not routinely be prescribed in primary care.

4.2.7 Prescription writing requirements for Schedule 3 controlled drugs

- Following concerns about abuse, gabapentin and pregabalin have been reclassified as a Class C controlled substances and Schedule 3 controlled drugs in 2019. Tramadol was re-classified as a Schedule 3 controlled drug in 2014.
- As per BNF online recommendations prescription for controlled drugs (including schedule 3) must be indelible, signed by the prescriber, include the date on which it was signed, and specify the prescriber's address (must be within UK).
- A machine-written prescription is acceptable, but the prescriber's signature must be handwritten.
- Advanced electronic signatures can be accepted for schedule 3 controlled drugs where electronic prescribing service (EPS) is used.
- All prescriptions for controlled drugs that are subject to the prescription requirements must always state:

    - The name and address of the patient
    - Form of the controlled drug must be specified (e.g., tablets)
    - For liquids, the total volume in millilitres (in both words and figures) must be specified (e.g., one hundred (100) millilitres')
    - For dosage units (e.g., tablets, capsules) total number (in both words and figures) must be stated (e.g., 'fifty-six (56) capsules')
    - Dose must be clearly defined (e.g., 'one capsule every 6 hours as directed)'. 'As directed' alone is not acceptable
    - If prescribed by a dentist 'for dental treatment only' must be included
    - The Department of Health and Social Care has issued strong recommendations that the maximum quantity of Schedule 3 drugs prescribed should not exceed 30 days
    - A prescription for controlled drug in schedule 3 is valid 28 days and is not repeatable

- For more information on prescribing Schedule 3 controlled drugs via Electronic Prescription Service (EPS) please see NHS Digital.

- Healthcare professionals should evaluate patients carefully for a history of drug abuse before prescribing gabapentin or pregabalin and observe patients for signs of abuse and dependence. Patients should be informed of the potentially fatal risks of interactions between gabapentin and alcohol, and with other medicines that cause CNS depression, particularly opioids.

4.3 Trigeminal neuralgia

- If there are red flag symptoms and signs that may suggest a serious underlying cause, admit, or refer urgently for specialist assessment, using clinical judgement e.g.:
    - Sensory changes
    - Deafness or other ear problems
    - History of skin or oral lesions that could spread perineurally
    - Pain only in the ophthalmic division of the trigeminal nerve (eye socket, forehead, and nose), or bilaterally
    - Optic neuritis
    - Family history of multiple sclerosis
    - Age of onset before 40 years

4.3.1 Offer carbamazepine as initial treatment

If there are no red flag symptoms and signs, offer carbamazepine as initial treatment for trigeminal neuralgia. Carbamazepine is licensed for the paroxysmal pain of trigeminal neuralgia in adults.

- Start at 100 mg twice daily and slowly titrate the dosage up in steps of 100mg - 200mg every two weeks, until pain is relieved
- In the majority of people, a dosage of 200 mg three or four times a day is sufficient to prevent paroxysms of pain (maximum dosage 1600 mg daily).
- Modified-release preparations may be useful at night if the person experiences breakthrough pain.
- Early follow up should be arranged to assess the progress made with dose titration, and the tolerability and effectiveness of the treatment. Clinical judgement to be used to decide how soon to follow up the patient.
- FBC and LFTs should be monitored during treatment with carbamazepine
- Once pain is in remission, the dosage should be gradually reduced to the lowest possible maintenance level, or the drug can be discontinued until a further attack occurs.
- Carbamazepine is associated with a number of cautions and drug interactions; prescribers are directed to consult individual SPCs.
- Follow the MHRA safety advice on antiepileptic drugs in pregnancy.

4.3.2 Consider expert advice

Consider referring the person to a specialist pain service or a neurologist at any stage, if:

- They have severe pain.
- Their pain significantly limits their participation in daily activities (including self-care, general tasks and demands, interpersonal interactions and relationships, mobility, and sleeping).
- The person has atypical clinical features (for example burning pain between paroxysms, loss of sensation, or any abnormal neurological signs).

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; **do not offer any other drug treatment unless advised to do so by a specialist.**

4.4 Sciatica

- If there are red flag symptoms and signs that may suggest a serious underlying cause, admit or refer urgently for specialist assessment using clinical judgement., e.g.,

    - Bowel/bladder dysfunction (most commonly urinary retention)
    - Progressive neurological weakness
    - Saddle anaesthesia
    - Bilateral radiculopathy
    - Incapacitating pain
    - Unrelenting night pain
    - Use of steroids or intravenous drugs

4.4.1 Pharmacological treatment

As per NICE guideline NG59 and NICE CKS on sciatica:

- Do not offer gabapentinoids, other antiepileptics, oral corticosteroids or benzodiazepines for managing sciatica as there is no overall evidence of benefit and there is evidence of harm
- Do not offer opioids for managing chronic sciatica
- If a person is already taking opioids, gabapentinoids or benzodiazepines for sciatica, discuss the problems associated with withdrawal with the person (also see GMMMG Gabapentinoids resource pack, GMMMG Benzodiazepine and Z-drug resource pack and/or GMMMG Opioid prescribing resource pack for further information)
- Be aware of the risk of harms and limited evidence of benefit from the use of non-steroidal anti-inflammatory drugs (NSAIDs) in sciatica
- If prescribing NSAIDs for sciatica: take into account potential differences in gastrointestinal, liver and cardio-renal toxicity, and the person's risk factors, including age; think about appropriate clinical assessment, ongoing monitoring of risk factors, and the use of gastroprotective treatment; use the lowest effective dose for the shortest possible period of time

5. Treatments not supported for use unless advised by specialist

5.1 The following drugs are not recommended by NICE CG173 for the treatment of neuropathic pain in primary care, owing to a lack of consistent evidence for their effectiveness, evidence of inferiority compared with placebo or other treatments, and/or evidence of a higher risk of adverse effects compared with other drugs. These drugs should not be routinely prescribed unless advised by a specialist to do so.

- **capsaicin patch**
- **cannabis sativa extract**
- **lacosamide**
- **lamotrigine**
- **levetiracetam**
- **morphine**
- **oxcarbazepine**
- **topiramate**
- **tramadol (long-term use)**
- **venlafaxine**
- **sodium valproate**

5.2 Capsaicin patch is listed by GMMMG as GREY/RED drug which can be used only in adults with post-herpetic neuralgia (PHN) who have not achieved adequate pain relief from, or who have not tolerated, conventional first and second-line treatments. It is listed as 'Do Not Prescribe' (DNP) by GMMMG for off-label indications.

5.3 Cannabis sativa extract is listed by GMMMG as DNP for neuropathic pain.

5.4 Lacosamide, levetiracetam, oxycodone and venlafaxine do not appear to be more effective than placebo or there is a lack of evidence and/or inconsistent evidence about whether they are better than placebo at reducing pain.

5.5 Sodium valproate should only be used in women in line with the MHRA regulatory measures around pregnancy prevention. Full information can be accessed from https://www.gov.uk/guidance/valproate-use-by-women-and-girls

5.6 Whilst the above list applies primarily to primary care; it is important to note that there is lack of consistent evidence for their effectiveness, in neuropathic pain. They should therefore be reserved for use after other standard treatments have failed. If any of the treatments discussed above are used in a specialist setting, then there should be clear documentation of benefit for that individual patient prior to continuing therapy.

5.7 If clear evidence of continuing benefit (e.g., a reduction in the neuropathic pain scale) for the patient is not supplied to primary care then secondary care will be expected to continue prescribing until such information can be supplied.

6. Information for Patients

What is neuropathic pain?

- Neuropathic pain happens when the nerves don't work properly and send the wrong signals to the brain.
- A common cause is a trapped nerve, for example, in the back or neck. Neuropathic pain can also be caused by conditions such as diabetes, shingles or by a painful nerve in the face (trigeminal neuralgia). Neuropathic pain can sometimes occur after a stroke, after amputation of an arm or a leg, and in people with cancer or multiple sclerosis.
- It can feel like shooting, stabbing, an electric shock, burning, tingling, tight, numb, prickling, itching or a sensation of pins and needles. The pain can come and go or be there all the time.
- Because the causes of neuropathic pain can be complicated and difficult to treat, it is often not possible to completely cure the source of the pain.

What are the treatments for neuropathic pain?

- **Neuropathic pain can be very painful and troublesome. Medicines might only partly help the symptoms.**
- Treatment might include non-drug options such as physiotherapy to help strengthen muscles. If you have diabetes, then making sure it is well controlled may help improve the pain, or at least stop it getting worse.
- Neuropathic pain is not like pain caused by a pulled muscle or a sprain, so the medicines used to treat it are different from common painkillers like paracetamol and ibuprofen. Medicines used to treat neuropathic pain are different in both the way that they work, and how long they take to work.
- To begin with, your doctor might prescribe you a drug called amitriptyline, gabapentin, pregabalin, or duloxetine. These are sometimes also used for treating other health conditions, such as depression, epilepsy, anxiety or headaches. When deciding on the best choice for you, your doctor will consider any other health problems you may have and any other medications you might be taking.
- When you start drug treatment for neuropathic pain it will usually be at a low dose, which is then increased gradually until you get the most benefit. Some people find that the dose can't be increased because they get side effects that are difficult to manage. Some people do not get any benefit from drug treatments, if this is the case the drug should be stopped gradually. For some patients changing to a different drug might be an option. It is not usually recommended to be on more than one treatment for neuropathic pain.
- The most common side effects are tiredness, dizziness, or feeling "drunk". If you get these, it may be necessary to reduce your dose. The side effects should improve after a week or two as your body gets used to the medicine. Do not drive or operate machinery if you experience drowsiness or blurred vision. You also may become more sensitive to the effects of alcohol.
- Some people who take pregabalin or gabapentin become physically dependent after long-term use. This means they experience withdrawal symptoms when they stop taking the medicine. If you are concerned about physical dependence with these medicines, then speak to your doctor or pharmacist
- Everyone is different and responds differently to drug treatment – some people find that the drugs start to help straight away, and for others it takes a bit more time. It is important to keep talking to your doctor about how you are feeling, whether things are improving, and what you can do to help yourself.

Adapted from: NICE CG173 Neuropathic pain in adults: pharmacological management in non-specialist settings 'Information for the public' September 2020.

Patient information- medicine specific

NHS.UK: *Amitriptyline - for pain and migraine*
https://www.nhs.uk/medicines/amitriptyline-for-pain/

Faculty of Pain Medicine: *Information for Adult Patients Prescribed Amitriptyline for the Treatment of Pain* (Leaflet)
https://www.britishpainsociety.org/british-pain-society-publications/patient-publications/

NHS.UK: Nortriptyline – for nerve pain and depression
https://www.nhs.uk/medicines/nortriptyline/

Faculty of Pain Medicine: *Information for Adult Patients Prescribed Nortriptyline for the Treatment of Pain* (Leaflet)
https://www.britishpainsociety.org/british-pain-society-publications/patient-publications/

NHS.UK: *Gabapentin*
https://www.nhs.uk/medicines/gabapentin/

Faculty of Pain Medicine: *Information for Adult Patients Prescribed Gabapentin for the Treatment of Pain* (Leaflet)
https://www.britishpainsociety.org/static/uploads/resources/files/FPM-Gabapentin_0.pdf

NHS.UK: *Pregabalin*
https://www.nhs.uk/medicines/pregabalin/

Faculty of Pain Medicine: *Information for Adult Patients Prescribed Pregabalin for the Treatment of Pain* (Leaflet)
https://www.britishpainsociety.org/static/uploads/resources/files/FPM-Pregablin_2.pdf

NHS.Uk: *Duloxetine*
https://www.nhs.uk/medicines/duloxetine/

Faculty of Pain Medicine: *Information for Adult Patients Prescribed Duloxetine for the Treatment of Pain* (Leaflet)
https://www.britishpainsociety.org/static/uploads/resources/files/FPM-Duloxetine_0.pdf

Patient information- general resources

The British Pain Society: Patient Publications
https://www.britishpainsociety.org/british-pain-society-publications/patient-publications/

Pain UK
Find out about other organisations helping people living with pain.
www.painuk.org

Pain Concern UK
https://painconcern.org.uk/product-category/leaflets/

7. References

1. International Association for the Study of Pain. Classification of Chronic Pain, Second Edition (Revised). Part III: Pain Terms: A Current List with Definitions and Notes on Usage. Available from https://www.iasp-pain.org/PublicationsNews/Content.aspx?ItemNumber=1673. Accessed June 2021.

2. National Institute for Health and Care Excellence (NICE), CG173, Neuropathic pain in adults; pharmacological management in non-specialist settings], November 2013 (last updated September 2020) http://guidance.nice.org.uk/CG173 Accessed June 2021.

3. NICE, Clinical Knowledge Summaries: Neuropathic pain – drug treatment. Last revised December 2020. https://cks.nice.org.uk/neuropathic-pain-drug-treatment#!scenario. Accessed June 2021.

4. NICE, Clinical Knowledge Summaries: Trigeminal Neuralgia – Management. Last revised January 2018. https://cks.nice.org.uk/trigeminal-neuralgia#!scenario. Accessed June 2021.

5. NHS England. Rescheduling of Gabapentin and Pregabalin as Schedule 3 Controlled Drugs: Guidance for urgent action. March 2019, https://www.cambridgeshireandpeterboroughccg.nhs.uk/easysiteweb/getresource.axd?assetid=17402&type=0&servicetype=1 Accessed December 2021.

6. Safer Prescribing in Prisons: Guidance for Clinicians – RCGP secure environments group (November 2011) https://www.rcgp.org.uk/clinical-and-research/resources/a-to-z-clinical-resources/~/media/106D28C849364D4CB2CB5A75A4E0849F.ashx

7. Galer S.G and Jensen M.P, Development and preliminary validation of a pain measure specific to neuropathic pain: The Neuropathic Pain Scale, Neurology 1997;48;332 https://n.neurology.org/content/48/2/332 . Accessed June 2021

8. NICE guideline NG193, Chronic pain (primary and secondary) in over 16s: assessment of all chronic pain and management of chronic primary pain, April 2021. https://www.nice.org.uk/guidance/ng193 Accessed September 2021

9. BNF online, Nortriptyline, retrieved on the 26.11.2021

10. BNF online, Neuropathic pain, retrieved on the 26.11.2021

11. GMMMG, Gabapentinoids – prescribing for pain, Resource pack, v1.0, 2021

12. BNF online, Controlled drugs and drug dependence, retrieved on the 25.02.2022

13. NICE guideline NG59, Low back pain and sciatica in over 16s: assessment and management, December 2020. https://www.nice.org.uk/guidance/ng59 Accessed February 2022

14. NICE CKS, Sciatica (lumbar radiculopathy), October 2021. https://cks.nice.org.uk/topics/sciatica-lumbar-radiculopathy/ Accessed February 2022

8. Appendix 1

Neuropathic pain scale

There are scales for measuring different aspects of pain. For one patient, a pain might feel extremely hot, but not at all dull, while another patient may not experience any heat, but feel like their pain is very dull. We expect you to rate very high on some of the scales below, and very low on others. We want you to use the measures that follow to tell us exactly what you experience.

1. Please use the scale below to tell us how **intense** your pain is. Place an "X" through the number that best describes the intensity of your pain.

0	1	2	3	4	5	6	7	8	9	10

No pain — The most intense pain sensation imaginable

2. Please use the scale below to tell us how **sharp** your pain feels. Words used to describe "sharp" feelings include "like a knife," "like a spike," "jabbing" or "like jolts."

0	1	2	3	4	5	6	7	8	9	10

Not sharp — The sharpest sensation imaginable ('like a knife')

3. Please use the scale below to tell us how **hot** your pain feels. Words used to describe very hot pain include "burning" and "on fire."

0	1	2	3	4	5	6	7	8	9	10

Not hot — The hottest sensation imaginable ('on fire')

4. Please use the scale below to tell us how **dull** your pain feels. Words used to describe very dull pain include "like a dull toothache," "dull pain," and "like a bruise."

0	1	2	3	4	5	6	7	8	9	10

Not dull — The most dull sensation imaginable

5. Please use the scale below to tell us how **cold** your pain feels. Words used to describe very cold pain include "like ice" and "freezing."

0	1	2	3	4	5	6	7	8	9	10

Not cold — The most cold sensation

imaginable ('freezing')

6. Please use the scale below to tell us how **sensitive** your skin is to light touch or clothing. Words used to describe sensitive skin include "like sunburned skin" and "raw skin."

0	1	2	3	4	5	6	7	8	9	10

Not sensitive

The most sensitive sensation imaginable ('raw skin')

7. Please use the scale below to tell us how **itchy** your pain feels. Words used to describe itchy pain include "like poison oak" and "like a mosquito bite."

0	1	2	3	4	5	6	7	8	9	10

Not itchy

The itchiest sensation imaginable

8. Which of the following best describes the time quality of your pain? **Please tick only one answer.**

( ) I feel a background pain <u>all of the time</u> and occasional flare-ups (break-through pain) <u>some of the time.</u>

Describe the background pain: _____

_____

_____

_____

Describe the flare-up (break-through) pain: _____

_____

_____

_____

( ) I feel a single type of pain <u>all the time</u>. Describe this pain: _____

_____

_____

_____

( ) I feel a single type of pain only <u>sometimes</u>. Other times, I am pain-free.

Describe this occasional pain: _____

_____

_____

_____

9 . Now that you have told us the different physical aspects of your pain, the different types of sensations, we want you to tell us overall how **unpleasant** your pain is to you. Words used to describe very unpleasant pain include “miserable” and “intolerable.” Remember, pain can have a low intensity, but still feel extremely unpleasant, and some kinds of pain can have a high intensity but be very tolerable.

With this scale, please tell us how unpleasant your pain feels.

0	1	2	3	4	5	6	7	8	9	10

Not unpleasant — The most unpleasant sensation Imaginable (‘intolerable’)

10. Lastly, we want you to give us an estimate the severity of your **deep** versus **surface** pain. We want you to rate each location of pain separately. We realise that it can be difficult to make these estimates, and most likely it will be a “best guess,” but please give us your best estimate.

How intensive is your deep pain?

0	1	2	3	4	5	6	7	8	9	10

No deep pain — The most intense deep pain sensation imaginable

How intensive is your surface pain?

0	1	2	3	4	5	6	7	8	9	10

No deep pain — The most intense surface pain sensation imaginable