

# Management of Neuropathic Pain for Adults in Primary Care

Does the patient have neuropathic pain?  
See pages 2-3. Consult specialist in pain medicine if unsure.

## Disturbed sleep or mood alteration

Consider:

- Sleep restoration strategies
- Cognitive behavioural strategies
- Tricyclic antidepressant

## Pharmacological Management

- See page 3 for information regarding realistic expectation of pharmacological management.
- Ensure adequate doses are trialled for a long enough time before moving to the next step. Do not continue ineffective treatment i.e. use “short sequential trials” or “one medication at a time”.
- Document baseline and set desired treatment outcomes prior to initiating therapies.
- Refer to BNF and/or SPC for adverse effects and contraindications for specific medications.

## Non-pharmacological treatment options

- Address common psychological co-morbidities (e.g. anxiety/depression)
- Physiotherapy
- Interventional approaches

## Misuse potential with pregabalin & gabapentin

Use with caution in patients with a personal or family history of substance / alcohol misuse; patients with mental health problems; and patients who have experienced a recent life event (including serious injury).

## Potential interaction with gabapentin and opioids.

Case controlled study showed increased risk of opioid related death when gabapentin given with opioids. Could be a class effect.

## Gabapentin (Neurontin): risk of severe respiratory depression (MHRA)

Gabapentin — rare risk of severe respiratory depression even without concomitant opioids. Patients at higher risk: compromised respiratory function, respiratory or neurological disease, renal impairment, concomitant use of central nervous system (CNS) depressants, and elderly people. Dose adjustments might be necessary in these patients. Could be a class effect.

Is the patient responding to and tolerating simple analgesics?

Paracetamol 1g QD and / or  
Ibuprofen 400mg TDS and / or  
Codeine Phosphate 30-60mg QDS

NO

## AMITRIPTYLINE trial (see \* for trigeminal neuralgia)

Start with low dose (10mg - 25mg) at night and titrate to 75mg at night if tolerated. Review after 6-8 week trial

\* For trigeminal neuralgia consider carbamazepine first line - 100mg BD increasing to 200mg QDS.

Has there been a significant decrease in pain AND substantial increase in physical function?

NO

Stop AMITRIPTYLINE

## GABAPENTIN trial

Follow [BNF](#) titration or slower. Aim for 600mg TDS (if CrCl<80ml/min see dosing table on pg 1 of main guideline). Review after 6-8 week trial.

Has there been a significant decrease in pain AND substantial increase in physical function?

NO

Stop GABAPENTIN

Other pharmacological treatment options to consider:  
**Duloxetine (Cymbalta®)** - 30mg each morning increased to 60mg daily after 2 weeks. Review after 8 week trial.

Avoid if CrCl<30ml/min. Caution hypertension/CVD, avoid abrupt withdrawal.

OR

**Pregabalin** - consider only if gabapentin provided some analgesic benefit but intolerable side effects. 75mg BD increased to max. 300mg BD as per BNF titration or slower.

**Tramadol** - consider for short periods only, 50-100mg QDS.

**Capsaicin 0.075% cream** - for post herpetic neuralgia, 3 to 4 times a day.

Has there been a significant decrease in pain AND substantial increase in physical function?

YES

YES

YES

Maintain on medication and dose that is working and review regularly

YES

NO

## Consider Referral to Specialist Pain Management Service

**Specialist pain team recommendation only:** Lidocaine 5% medicated plasters for localised neuropathic pain due to post herpetic neuralgia (PHN) only where oral treatments and capsaicin have been ineffective or are contraindicated.

## Management of Neuropathic Pain for Adults in Primary Care

### SCOPE

This prescribing guideline is to assist primary care prescribers in treating patients with neuropathic pain BEFORE referral to specialist services.

### UNDERSTANDING NEUROPATHIC PAIN

Neuropathic pain is very different from inflammatory pain. Whilst nociceptive pain is produced by tissue damage neuropathic pain is caused by a lesion or disease affecting the somatosensory nervous system which can result from nerve damage caused by trauma or certain conditions (see below).

### CAUTIONS WITH NEUROPATHIC PAIN THERAPIES

- Use pain medication with caution in patients who are frail, elderly or who have cardiac disease.
- Many medicines recommended are not licensed for the treatment of neuropathic pain.
- Only use opioids (including codeine doses greater than 120mg daily) as part of comprehensive management plan and regularly review (see below). Refer to the [APC guidance on the use of opioids for persistent non-cancer pain](#) and the Faculty of Pain Medicine [Opioids Aware](#) resource.
- Cases of Gabapentin and pregabalin misuse are increasing. Use both with caution for patients with a personal or family history of substance or alcohol misuse.
- Gabapentin — rare risk of severe respiratory depression even without concomitant opioid medicines (ref: MHRA Oct17). Patients at higher risk are those with compromised respiratory function, respiratory or neurological disease, renal impairment, concomitant use of central nervous system (CNS) depressants, and elderly people. Dose adjustments might be necessary in these patients. Note that this could be a class effect and pregabalin may prove to have a similar effect on respiratory function.
- Risk of opioid related death increased with gabapentin and concomitant opioids (ref: [Gomes T at al](#)).
- **Gabapentin in renal impairment** (ref: Neurontin SPC):

Creatinine Clearance (ml/min)	Dose
≥80	300mg TDS to 1200mg TDS
50-79	200mg TDS to 600mg TDS
30-49	100mg TDS to 300mg TDS
15-29	300mg every other day to 200mg TDS
<15*	300mg every other day to 100mg TDS

\*For patients with creatinine clearance <15 mL/min, the daily dose should be reduced in proportion to creatinine clearance (e.g., patients with a creatinine clearance of 7.5 mL/min should receive one-half the daily dose that patients with a creatinine clearance of 15 mL/min receive).

- Other physical treatments (e.g. TENS, acupuncture, physiotherapy) may be beneficial.
- TENS only works while the machine is operational but may provide relief for short periods.

### HOW COMMON IS NEUROPATHIC PAIN?

- Neuropathic pain is a common condition affecting between 6% and 8% of the population.
- An average GP may have between 35 and 70 patients with neuropathic pain.
- Much neuropathic pain can be successfully managed within primary care.

\* For full prescribing information please see BNF and/or relevant Summary of Product Characteristics.

## RECOGNISING AND DIAGNOSING NEUROPATHIC PAIN

Common causes are:

- Diabetes Mellitus (type 1 and 2)
- Shingles (Herpes Zoster)
- Trigeminal Neuralgia
- Post Surgery e.g. post hernia repair
- Chronic spinal problems e.g. sciatica, neck pain, low back pain
- Underlying malignancy or other occult disease

### Referral Considerations:

Emergency	Urgent	Non-Urgent
Cauda equina syndrome	Infection	Metabolic causes e.g. alcohol excess or vitamin deficiency
	Cancer	Phantom limb pain
	Trauma	Post-surgery
		Medication toxicity e.g. chemotherapy
		Idiopathic

### Possible initial investigations if cause in doubt:

ESR, CRP, fasting glucose, glucose tolerance test, LFTs, FBC, Vitamin B<sub>12</sub> & folate, U&Es, TFTs

### Symptoms and signs of neuropathic pain:

- can be spontaneous or evoked; continuous or intermittent.
- is often worse at the end of the day.
- can be exacerbated by heat, cold or external stimulation - even simply wearing clothes or bed sheets.

## HISTORY

- Encourage patients to describe their pain sensation.
- Neuropathic pain may be characterized by unpleasant symptoms, such as:
  - shooting or burning pain
  - altered sensation
  - sensations (e.g. pins and needles) that are very difficult to describe
  - numbness
- However, many pains, including pain arising from classically “non-neuropathic” conditions (e.g. osteoarthritis or cancer pain), can have neuropathic characteristics.
- Pain that unresponsive to conventional analgesics (paracetamol, NSAIDs and weak opioids) may have neuropathic elements.
- Consider use of a validated questionnaire (e.g. S-LANSS or Pain Detect) to aid diagnosis of neuropathic pain.
- The Brief Pain Inventory (appendix 1) is useful to assess pain intensity and the impact that the pain is having on daily living.

## SENSORY SIGNS

- Allodynia - pain produced by an innocuous stimulus e.g. touch, pressure, warmth
- Dysaesthesia - an unpleasant, abnormal sensation
- Hyperaesthesia - an increased sensitivity to touch
- Hyperalgesia - an increased response to a stimulus which is normally painful

## ASSOCIATED SYMPTOMS AND SIGNS

- Reduced activity (65%)
- Poor sleep (60%)
- Depression (34%)
- Anxiety (25%)

\* For full prescribing information please see BNF and/or relevant Summary of Product Characteristics.

## PREVENTION & EARLY MANAGEMENT OF NEUROPATHIC PAIN

- Diabetes - Ensure optimal glycaemic control to minimise peripheral diabetic neuropathy.
- Herpes zoster - Neuropathic pain medication given in the acute phase may reduce post-herpetic neuralgia but are unproven.

## MANAGEMENT

- Management of neuropathic pain should use a holistic biopsychosocial model that also addresses underlying psychological and social issues.
- If the diagnosis is uncertain consider early referral to a specialist.

## MANAGING EXPECTATION OF PHARMACOLOGICAL TREATMENTS

- It is essential that prescribers and patients have realistic expectations for treatment.
- Development of self-management skills (see [Pain Toolkit](#)) in combination with pharmacological treatment options is essential.
- Treatment outcomes (reduction in pain intensity or pain relief and functional outcomes) should be agreed and documented prior to initiation of treatments for neuropathic pain.
- Analgesics for neuropathic pain are unlikely to provide complete pain relief, however a successful trial should provide at least 50% reduction in pain intensity.
- Those patients who do gain good pain relief often experience improvements in other physical and psychological domains (e.g. sleep, mood, quality of life).
- Effects are unlikely to be noticeable for up to two weeks after initiation but the maximum benefit may not be observed until 6-8 weeks, however patients may experience side effects much sooner.
- Most side effects are relatively minor and will resolve if the patient is able to persist in taking for the medicine several weeks.
- Reassessment of effectiveness by a gradual dose reduction at least once a year is advised to ensure that medicines are continuing to provide benefit.

## IMPROVING CONCORDANCE

- Explain the reason and rationale for your treatment choices.
- Explain commonly used medicines (e.g. antidepressants and antiepileptics) may be used for another condition.
- Explain common side effects.
- Explain timescale expected for improvement and possible next step.
- The British Pain Society has a useful patient information leaflet about persistent pain [here](#) and the Faculty of Pain Medicine has patient information leaflets about medicines for neuropathic pain [here](#).

## REVIEW

Patients should be followed closely to review diagnosis and ensure that the treatment is titrated to the response. At each review consider: the diagnosis, efficacy and tolerability of medication and whether the dose adjustment is required. Once stabilised on treatment patients should be reviewed at least annually.

The Brief Pain Inventory in appendix 1 is a useful tool to monitor the effect of management.

Refer patient to specialist at any stage – where the diagnosis is in doubt or patient is not responding to treatment.

\* For full prescribing information please see BNF and/or relevant Summary of Product Characteristics.

## Pharmacological Management – prescribing information\* (dosing and titration)

Medicine	Typical daily starting dose	Maximum daily dose	Comments	Approx. cost per 28 days at max. dose	Duration of adequate trial
<b>TRICYCLIC ANTIDEPRESSANTS</b>					
Amitriptyline	10 – 25 mg at night	75 mg at night	Take 90 – 120 minutes before going to bed. Response normally evident at 75 mg daily, however doses up to 150 mg at night may be used to optimise response. Do not stop abruptly – gradually titrate down. Only use Nortriptyline if amitriptyline effective but not tolerating side effects. <b>OFF-LABEL INDICATION</b>	£2.22	6 – 8 weeks with at least 2 weeks at maximum tolerated dose
<b>ANTI-EPILEPTICS</b>					
Carbamazepine	100 mg BD	200 mg QDS	For initial treatment of <b>trigeminal neuralgia</b> . Increase slowly to 200mg 2-4times daily. Avoid sudden withdrawal - gradually titrate down.	£5.11	6 – 8 weeks with at least 2 weeks at max. tolerated dose
Gabapentin	300 mg ON	600 mg TDS	See <a href="#">BNF</a> for suggested titration regimen. Side effects worst at times of dose increase. Do not stop abruptly – gradually titrate down. See SPC for dosing if CrCl is less than 80ml/min. <a href="#">APC statement re gabapentin and pregabalin misuse</a>	£5.42	3 – 8 weeks for titration plus two weeks at maximum dose
Pregabalin	75mg BD	300mg BD	As gabapentin. Only if gabapentin ineffective or not tolerating gabapentin. Do not stop abruptly – gradually titrate down. <a href="#">Caution if history of substance or alcohol misuse.</a>	£5.50	4 weeks
<b>SNRI</b>					
Duloxetine	30mg OD (for 2 weeks then increase to 60mg OD)	60 mg OD (but see comments)	Licensed for diabetic neuropathy only. Avoid in severe renal impairment (CrCl<30ml/min). Avoid abrupt withdrawal (withdraw slowly over min. of 1 to 2 weeks). Risk of serotonin syndrome if used concomitantly with other serotonergic agents. Blood pressure monitoring recommended in patients with known hypertension and/or other cardiac disease, especially during first month. May have small increase in fasting glucose / HbA1c. May increase LFTs.  The plasma concentration of duloxetine displays large inter-individual variability. Hence, some patients that respond insufficiently to 60 mg may benefit from a higher dose (max 60mg BD).	£11.57	8 weeks
<b>OPIOIDS</b>					
Tramadol	50 – 100 mg QDS	100 mg QDS	Consider tramadol for short periods only, not for long term use (NICE CG173). Increased risk of seizure / serotonin syndrome when used in conjunction with TCA or SSRI. May cause less respiratory depression and constipation than opioids.	£4.93	4 weeks
<b>TOPICAL AGENTS for Post Herpetic Neuralgia (PHN)</b>					
Capsaicin	0.075%	3 – 4 times daily	For post herpetic neuralgia. Care on application (see patient information leaflet). Counselling required. Review at 8 weeks and only continue if benefit is seen.	£14.58	8 weeks
Lidocaine 5% medicated plaster	One plaster (can be cut)	Three plasters	Nottinghamshire Traffic Light classification – <b>Amber 2 - on Pain Management Service recommendation only for localised neuropathic pain due to post herpetic neuralgia (PHN) only where oral treatments and capsaicin have been ineffective or are contraindicated.</b> Up to three plasters to be applied for 12 hours each day. Review after 4 weeks and unless there is a significant decrease in pain or substantial increase in physical function then it should be stopped.	£217.20	4 weeks

\* For full prescribing information please see BNF and/or relevant Summary of Product Characteristics.

## REFERENCES

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\* For full prescribing information please see BNF and/or relevant Summary of Product Characteristics.

## Appendix 1 – Pain inventory

Pain Detect <http://www.specialistpainphysio.com/wp-content/uploads/2010/07/painDETECT-Questionnaire-01.pdf>

Brief Pain Inventory <http://www.hnehealth.nsw.gov.au/Pain/Documents/BPI.dec06.pdf>

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