

Neuropathic pain management pathway (LANSS score 12 or above)

Consider Capsaicin 0.075% cream for people with **localised** neuropathic pain (off-label) who wish to avoid, or who cannot tolerate; oral treatments.

1

Amitriptyline

Advise pt. may take 6-8 weeks to reach therapeutic dose
Review 8 weeks after initiating

- Initiate at 10mg each evening and titrate weekly in increments of 10mg daily until either efficacy is achieved or patient cannot tolerate the drug.
- 50 - 75mg is usual therapeutic dose range for neuropathic pain
- If < 8 weeks treatment, withdrawal effects unlikely. ≥ 8 weeks: wean off over 4 weeks

Contra-indicated, ineffective or not tolerated

30-50% reduction in symptoms: See notes below for exit strategy

2

Stop amitriptyline, start gabapentin

*Use 300mg caps EXCEPT in frail elderly or those with eGFR 30 – 80 mL/min use 100mg caps. Max adult dose 3.6g/day
Because of the slow dose titration, an adequate trial may take more than 2 months

Gabapentin initiation	Morning	Lunchtime	Night
Titrate by number of capsules* in the table below, assessing every 2-4 weeks until either effective dose reached or unable to tolerate. Consult product literature for dose if eGFR <30mL/min			
Days 1 – 3			1
Days 4 - 6	1		1
Days 7 - 21	1	1	1
Week 4 - 5	1	1	2
Week 6 - 8	2	1	2
Weeks 9 - 10	2	2	2
Weeks 11 - 12	2	2	3
Weeks 13 - 14	3	2	3
Weeks 15 - 16	3	3	3

Contra-indicated, ineffective or not tolerated

30-50% reduction in symptoms: See notes below for exit strategy

3

Stop gabapentin, start duloxetine

Advise pt. may take 6-8 weeks to reach therapeutic dose and assess efficacy
Review pt 8 weeks after initiating

Cross weaning gabapentin to duloxetine

Gabapentin	Duloxetine
Reduce dose by 300mg every 4 days	Initiate at 30mg daily, increase to 60mg daily when gabapentin dose is at least halved After 8 weeks , review efficacy and titrate up to maximum 60mg BD

Contra-indicated, ineffective or not tolerated

30-50% reduction in symptoms: See notes below for exit strategy

- Stop any TCA and withdraw SSRI if taking (Seek advice from medicines optimisation team if required)
- **Duloxetine is licensed for diabetic neuropathic pain**

- Re-assess diagnosis and assess and treat any concomitant anxiety / depression
- Consider physiotherapy referral
- Consider combination therapy with two agents where **some** response was seen (need to consider interactions)
- Review if previous steps were titrated appropriately – slowly to avoid side effects and to a dose / duration likely to achieve efficacy
- If all of above steps have been actioned, refer patient to secondary care for consideration of pregabalin (consultant initiation only). See section D below for details on continuation of prescribing.

Consider other clinical conditions the patient may be presenting with or being treated for, e.g. depression where withdrawal or switching may be inappropriate without specialist advice.

Expected benefit of treatment:

A. Agreeing treatment outcomes

Without managing expectations, people with neuropathic pain may assume a 100% response following treatment initiation, which is rarely achieved. A likely improvement of 30-50% of neuropathic pain symptoms within approximately eight weeks is suggested and patients should be counselled of this expectation.

- Consider using the BPI questionnaire for a baseline global assessment of symptoms (and for re-assessing)
- Agree an achievable pain relief goal (e.g. 50% pain relief or ability to undertake global activities)
- Advise patient on the medication, titration regimen (see drug specific information below) and target dose.
- Prescribe on acute prescriptions (not repeat) until treatment is stabilised.
- Review all treatments after 8 weeks once the dose is titrated to an adequate dose. Discontinue treatments that are ineffective. Consider other clinical conditions the patient may be presenting with or being treated for, for example depression where withdrawal or switching may be inappropriate without specialist advice.
- Ongoing review: treatment should be reviewed regularly for continued need. Discontinue repeats for medication no longer being taken.

B. Choice of agent:

A recent systematic review and meta-analysis concluded that tricyclic antidepressants, duloxetine, gabapentin or pregabalin could all be recommended as first-line treatments in neuropathic pain.

NICE guideline development group for neuropathic pain proposed that treatments for neuropathic pain are offered in a sequential order of cost efficacy, with amitriptyline and gabapentin for initial therapy. Pregabalin and duloxetine were recommended as initial treatment options due to their wider licences; however the GDG did acknowledge that both these treatments represented poor value for money and further states:

“Probabilistic sensitivity analysis showed a negligible probability that either of these options provides greatest net benefit at conventional QALY values. For these reasons, the GDG felt it would not be possible to support recommendations that suggested either option as an initial treatment for neuropathic pain. However, the GDG noted that, when compared with placebo alone (that is, no treatment), both drugs appeared to be viable options from a health economic point of view. Therefore, it would be appropriate to recommend these treatments in a context where other options were removed from the decision-space – that is, when they are contraindicated or when they have been tried and proven ineffective or were not tolerated.”

NNTs (for 50% pain relief) were 7.7 for pregabalin and 7.2 for gabapentin. **The pharmacokinetic properties of pregabalin make the drug relatively more dangerous than gabapentin in high doses.** For this reason, and due to high local use compared to

similar CCGs, the system financial position, and the availability of alternative treatment options, pregabalin should not be initiated in primary care for any new patients for the management of neuropathic pain.

C. Trial withdrawal of successful treatment:

The goal of neuropathic pain treatment is to support initial symptom relief for people such that they are sufficiently able to engage in non-pharmacological treatment such as light exercise, physiotherapy, relaxation techniques and rehabilitation. Pharmacologic therapy should not be considered a long term management strategy and efforts should regularly be made to dose reduce or stop medicines, many of which are associated with safety or dependence issues following long-term use.

Once a patient has been stabilised on a treatment that has reduced their pain symptoms to their previously agreed pain relief goal, they should be maintained at this dose for approximately 3 months. During this time they should be encouraged to engage with non-pharmacological strategies.

After three months on a treatment that has maintained their pain symptoms to their previously agreed pain relief goal, dose reduction or withdrawal of treatment should be attempted. Consider other clinical conditions the patient may be presenting with or being treated for, for example depression where withdrawal or switching may be inappropriate without specialist advice.

Example proposed withdrawal regimens, where clinically appropriate, are described in the table below:

Amitriptyline	Reduce total daily dose by 10mg each week
Gabapentin (total daily dose > 900mg)	Reduce total daily dose by 300mg every week
Gabapentin (total daily dose ≤ 900mg)	Reduce total daily dose by 100mg every week
Duloxetine	Reduce daily dose by 30mg each week, following a week of 30mg daily, take 30mg on alternate days for 1 week and then stop
Pregabalin	Reduce total daily dose by 50mg every week*

*See also section below **“Switching from pregabalin to gabapentin”**

If complete withdrawal of treatment is not successful, patient should continue on the last dose in the reduction regimen at which pain was tolerable and they should be engaged in discussion about long term goals and non-pharmacologic management. Dose reduction or withdrawal should be reattempted on a bi-annual basis, if clinically acceptable.

D. Risk of dependence with gabapentin / pregabalin:

Pregabalin and gabapentin are associated with significant euphoric effects and misuse of these agents has been noted for some years. Individuals misusing them describe improved sociability, euphoria, relaxation and a sense of calm. Currently, pregabalin appears to be more sought after for misuse than gabapentin. There is a growing illegal market, and these drugs are also being bought through online pharmacies.

Gabapentin and pregabalin have the propensity to cause depression of the central nervous system, resulting in drowsiness, sedation, respiratory depression and at the extreme, death. Both gabapentin and pregabalin have adverse effects on the central nervous system, which are additive when used with other centrally acting drugs, particularly opioids. Gabapentin or pregabalin should not be co-prescribed with opioids and patients should be advised of the dangers of drinking alcohol while using these agents.

Pregabalin may have a higher abuse potential than gabapentin due to its rapid absorption and faster onset of action and higher potency.

E. Use of gabapentin / pregabalin in non-neuropathic pain:

Although gabapentin and pregabalin are commonly prescribed for non-neuropathic pain syndromes, e.g. fibromyalgia, chronic pain; there is little evidence to support the practice and use in non-neuropathic pain is off-label. Prescribers should consider interventions more likely to help such as physical rehabilitation.

For patients already established on treatment where pain does not appear to be neuropathic in nature (consider using questionnaires, i.e. [LANSS](#) and [PainDETECT](#)) and where this is not currently well controlled, gabapentin or pregabalin should be withdrawn (see table in section E) and alternative management plan agreed.

F. Switching from pregabalin to gabapentin:

Consider switching patients on pregabalin, whose neuropathic pain is not effectively managed; to amitriptyline, gabapentin or duloxetine if these medicines have not been tried previously, or the dose of treatment has not been previously titrated and maximised.

Review and switch from pregabalin to gabapentin should be undertaken for patients who have not previously tried these products or where previous dose-titration was sub-optimal, (especially for those patients whose neuropathic pain is not effectively managed). Community pharmacists should also be informed of any switch processes.

For example: pregabalin daily dose may be reduced by 50mg every 4 days. Initially, pregabalin dose should be reduced as per the table in section E, without adding in gabapentin. When patient reaches a dose at which pain is intolerable, convert the dose to gabapentin (50mg pregabalin \equiv 300mg gabapentin) and titrate back up to response using gabapentin (increasing by 300mg a day every 4 – 7 days) up to lowest dose that offers pain relief.