

Key Points to Remember

- Diagnosis: most neuropathic pain results from damage to nerves which may occur after tissue injury or CNS damage. It can be difficult to confirm. Pain is often described as shooting, stabbing, burning, gnawing or itching.
- Medication should be kept on the acute list, reviewed regularly and withdrawn if unsuccessful. If successful, aim to reduce and stop after 6 months. Only add to the repeat list where relevant after the 6 month review point.
- When withdrawing/changing treatment, taper appropriately to manage pain and avoid discontinuation symptoms.
- Discuss pain coping strategies and the importance of concurrent non-pharmacological management at each point, e.g. [The Pain Toolkit](#), self-management courses.
- **A 30% improvement in pain and a positive impact on daily activities is considered a successful outcome.**
- NICE do not make recommendations for combination therapy due to lack of evidence. Pregabalin and Gabapentin should NOT be prescribed together. The full NICE guideline for neuropathic pain can be found [here](#)

TREATMENT ALGORITHM

The recent classification of gabapentin and pregabalin to Schedule 3 controlled drugs, due to the risks of dependence, misuse and diversion, should be considered before making treatment decisions. Amitriptyline should be used first line where possible.

AMITRIPTYLINE* tablets

- Start at **10mg daily** and titrate by 10mg weekly according to side effects/response to max 70-75mg daily (as a single evening dose). Maximum tolerated dose should be used for 4 weeks before judging benefits.
- Less suitable for use in the elderly due to increased risk of side-effects, e.g. sedation and confusion.
- Care with drug interactions, including use with other antidepressants, and other comorbidities
- Avoid if suicide risk due to toxicity in overdose
- If satisfactory pain reduction but not tolerated – consider oral nortriptyline* as alternative

** Not licensed for neuropathic pain but the evidence for treatment efficacy and safety is deemed sufficient to make this recommendation.*

If initial treatment with amitriptyline is unsuitable, not tolerated or unsuccessful offer gabapentin (stop amitriptyline slowly)

GABAPENTIN* capsules

- Start at 300mg nocte (100mg if very frail/ susceptible to sedative medications) and titrate by 300mg daily (total in 3 divided doses) according to side effects/response to usual max 1.8g daily (licensed max 3.6mg)
- Once on maximum tolerated dose wait for 2 to 4 weeks to assess if there is a worthwhile benefit.
- Caution: potential for abuse, and risk of CNS/respiratory depression, particularly if co-prescribed with opioids. Consider carefully before prescribing if there is risk of drug misuse or diversion.

**Licensed for peripheral neuropathic pain only*

If initial treatment with gabapentin is unsuitable, not tolerated or unsuccessful (and amitriptyline has already been considered or tried) consider duloxetine or pregabalin (stop gabapentin slowly)^a

OR

DULOXETINE*

- Start 30mg daily and titrate to max 60mg BD according to response/side-effects. Consider lower starting doses in some patients.
- Nausea common on initiation but may resolve.

**Licensed for diabetic peripheral neuropathic pain only*

If either unsuitable, unsuccessful or not tolerated, stop slowly and consider remaining drug

PREGABALIN capsules

- Start at 75mg nocte and titrate according to side effects/response to max 600mg daily in **two** divided doses. Consider lower doses in the elderly (e.g.25mg BD)
- Once on maximum tolerated dose wait for 2 to 4 weeks to assess if there is a worthwhile benefit.
- Caution: potential for abuse, particularly if co-prescribed with opioids. Consider carefully before prescribing if there is risk of drug misuse or diversion.

^a**Note:** Gabapentin / Pregabalin: Weight gain can occur with both drugs and is not a reason to switch between gabapentin and pregabalin. If switching between these drugs no washout period is necessary.

See guidance notes on next page

Guidance Notes

Starting treatment and titrating drug dosages

Address concerns and expectations when agreeing which treatment(s) to use, **if any**. Discuss benefits, adverse effects, why a treatment is chosen, coping strategies, concurrent non-pharmacological management and access to this.

To avoid unrealistic expectations, agree realistic goals. Pain reduction of at least 30% is generally accepted to be a clinically meaningful result. Explain that this, together with improved function, may be achievable and worthwhile goals. Explain the importance of dosage titration and the titration process. When introducing a new treatment, consider overlap with the old treatment. With all agents, start at a low dose and titrate upwards to an effective, or maximum tolerated, dose. Medication should be kept on the patient's acute list, only adding to the repeat list, where relevant, after the 6 month review point.

How long is an adequate trial of a drug?

A trial of up to 2-3 months at the maximum tolerated dose should be adequate to assess efficacy. If **no meaningful benefit** has been derived during this time the drug should be stopped and another agent considered. Medication should always be withdrawn slowly.

Clinical reviews

After starting, increasing or changing treatment, perform an **early clinical review** to assess benefit, tolerability and adverse effects. Throughout treatment, **perform regular reviews** to monitor the effectiveness of treatment. Include assessment of pain reduction, adverse effects, impact on daily activities, mood, sleep quality and continued need for treatment. **Note:** For gabapentin and pregabalin, also observe for signs of abuse or dependence.

Duration, reducing and stopping treatment

If satisfactory improvement is achieved following introduction and upward titration of a drug, maintain the person on this dosage for a period of at least **six months**. Thereafter, aim to reduce the dose with a view to stopping treatment altogether. Dosage reduction should be carried out **very slowly**, with reductions at intervals of about two weeks (e.g. pregabalin 300mg twice daily could be reduced to 150mg in the morning and 300mg at night – for two weeks; then 150mg twice daily – for two weeks; then 75mg in the morning and 150mg at night – for two weeks, etc.). **If a drug cannot be stopped completely, it is important to attempt to reduce it to the lowest effective dose if to be used in the long-term.** Non-pharmacological/self management strategies should continue at all stages.

Dose Titration Schedules (according to response)

Amitriptyline

Morning	Noon	Evening	Duration
		10mg	1 week
		20mg	1 week
		30mg	1 week
		40mg	1 week
		50mg	1 week
		60mg	1 week
		70-75mg	

Gabapentin - Slow Titration

Morning	Noon	Evening	Duration
		100mg	3 days
100mg		100mg	3 days
100mg	100mg	100mg	3 days
300mg		300mg	7 days
300mg	300mg	300mg	7 days
300mg	300mg	600mg	7 days
300mg	600mg	600mg	7 days
600mg	600mg	600mg	

Gabapentin - Standard Titration

Morning	Noon	Evening	Duration
		300mg	3 days
300mg		300mg	7 days
300mg	300mg	300mg	7 days
300mg	300mg	600mg	7 days
300mg	600mg	600mg	7 days
600mg	600mg	600mg	

Pregabalin – Slow Titration

Morning	Noon	Evening	Duration
		25mg	3 days
25mg		25mg	1 week
50mg		50mg	1 week
75mg		75mg	1 week
150mg		150mg	1 week
300mg		300mg	

Pregabalin – Standard Titration

Morning	Noon	Evening	Duration
		75mg	1 week
75mg		75mg	1 week
150mg		150mg	1 week
300mg		300mg	

Other Treatments

Carbamazepine: recommended as initial treatment for trigeminal neuralgia. Serum sodium levels should be monitored due to possibility of hyponatraemia.

Opioids: Neuropathic pain is not particularly responsive to opioids. NICE do not recommend opioids unless advised by a specialist.

Tapentadol MR: Schedule 2 controlled drug and an opioid. It is not recommended for initiation in primary care. It may be recommended as a sole agent for mixed (neuropathic/nociceptive) pain **in a specialist setting**.

Tramadol: NICE recommend tramadol if acute rescue therapy is needed and **only for long term use if advised by a specialist**.

Lidocaine Plasters: Not recommended by NICE for neuropathic pain and have a limited place within the NI Formulary.

Capsaicin Cream: Option for localised pain if oral therapy is to be avoided/not tolerated.

Note: QT Prolongation. As with many medications, some neuropathic pain treatments may cause QT prolongation. These should be assessed along with other potential risk factors when initiating therapy. A useful summary can be found [here](#).