Implementation Support Tool for Non-Malignant Neuropathic Pain* in Non-Specialist Settings - *New Patients*

*Except Trigeminal Neuralgia

Health and Social Care Board

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Key Points to Remember

- Neuropathic pain is caused by a lesion or disease of the somatosensory nervous system. Pain is often described as shooting, stabbing, burning, gnawing or itching. It can be difficult to confirm — a validated tool should be used, e.g. LANSS Scale for Neuropathic Pain
- Medication should be reviewed regularly and withdrawn if unsuccessful. If successful, aim to reduce and stop after 6 months.
- **30% improvement in pain and a positive impact on daily activities is considered a successful outcome.**
- When withdrawing/changing treatment, taper appropriately to manage pain and avoid discontinuation symptoms.
- Do not prescribe more than one neuropathic pain drug at the same time, e.g. amitriptyline and gabapentin.
- Discuss pain coping strategies and the importance of concurrent non-pharmacological management at each point, e.g. The Pain Toolkit, self-management programmes.
- NICE guidance for managing neuropathic pain can be found here

TREATMENT ALGORITHIM

Due to increased deaths involving pregabalin, and the risks of dependence, misuse and diversion, pregabalin has been removed from the Northern Ireland Formulary for Neuropathic Pain. Patients on pregabalin should continue to be reviewed, and stepped down where appropriate.

Amitriptyline should be used first line where possible.

AMITRIPTYLINE tablets

- Initially 10–25 mg as a single evening dose, increased if necessary, according to response and tolerability, by 10–25 mg every 3–7 days to an effective, or maximum tolerated, dose. Max: 75 mg a day.
- Consider 6–8 week trial, with at least 2 weeks at the maximum tolerated dose, before deciding not effective.
- 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 unsuitable, not tolerated or unsuccessful offer gabapentin - stop amitriptyline slowly

GABAPENTIN* capsules

- Start 300mg at night on day 1, 300mg twice daily on day 2 , then titrate up in steps of 300mg daily (total dose given in 3 divided doses) according to side effects/response, to an effective, or maximum tolerated, dose: usual max:1.8g daily (Licensed max: 3.6g daily. If no substantial improvement at 2.4g, increasing the dose further is unlikely to be of benefit)
- Consider dose adjustments including lower starting dose [100mg - unlicensed] in the frail/elderly or if susceptible to sedative medications, e.g. compromised respiratory function, renal impairment and concomitant use of CNS depressants
- Wait for 2 to 4 weeks at maximum tolerated dose before deciding not effective.
- Caution: potential for abuse and risk of CNS/respiratory depression particularly if co-prescribed with opioids.
- Schedule 3 Controlled Drug (CD): consider risks of dependence, misuse and diversion before prescribing. In line with legislation, procedures must be in place for regular clinical review/monitoring.

**Licensed for peripheral neuropathic pain only*

If unsuitable, not tolerated or unsuccessful (and amitriptyline has already been considered or tried) consider duloxetine—stop gabapentin slowly[α]

DULOXETINE* capsules

- 60mg once daily, discontinue if inadequate response after 2 months; review at least 3 monthly; Lower starting dose of 30mg once daily may be appropriate in some people
- Licensing allows 60mg twice a day however not recommended due to unwanted effects/lack of benefit.
- Nausea is common on initiation but may resolve

**Licensed for diabetic peripheral neuropathic pain only*

See guidance notes and other treatments on next page

[α]Weight gain can occur with both gabapentin and pregabalin, and is not a reason to switch between these drugs .

Guidance Notes

Starting treatment and titrating drug dosages

Confirm diagnosis and record in the patient's notes. Address concerns and expectations when agreeing treatment, **if any.** Discuss benefits, adverse effects, why a treatment is chosen, concurrent non-pharmacological management strategies (and signpost accordingly), and plans for review and stopping treatment. To avoid unrealistic expectations, agree realistic goals. Pain reduction of 30% is generally a clinically meaningful result. Explain to patients that this, together with improved function, may be achievable and worthwhile goals. Explain the importance of dosage titration and the agreed titration process. With all agents, start at a low dose and titrate up to an effective, or maximum tolerated dose. Further information on managing neuropathic pain including starting and withdrawing treatment can be found here. Consider short term authorisation on the repeat list only where meaningful benefit has been demonstrated, and there is a robust system in place for review.

Clinical reviews

If **no meaningful benefit** is achieved following an adequate trial, the drug should be stopped (slowly) and another considered, as appropriate. After starting, increasing or changing treatment, perform an **early clinical review** to assess benefit, tolerability and adverse effects. Throughout treatment, **regular reviews** should be carried out to monitor efficacy, including assessment of pain, adverse effects, impact on daily activities, mood, sleep quality-and continued need for treatment. For gabapentin also check for signs of abuse/misuse or dependence.
Note: Gabapentin is a Schedule 3 controlled drug (CD). Procedures must be in place to ensure the regular clinical monitoring/review of all CDs.

Duration, reducing and stopping treatment

If satisfactory improvement is achieved following introduction and titration of a neuropathic 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. **The dose should be reduced very slowly, with reductions at intervals of about two weeks.** Pregabalin is no longer on the Northern Ireland formulary, however patients on pregabalin should continue to be reviewed and stepped down as appropriate.

Examples of Dose Titration Schedules (according to response)

Amitriptyline

Morning	Noon	Evening	Duration
		10mg	Step 1
		20mg	Step 2
		30mg	Step 3
		40mg	Step 4
		50mg	Step 5
		60mg	Step 6
		70-75mg	Step 7

Gabapentin - Slow Titration (e.g. elderly)

Morning	Noon	Evening	Duration
		100mg	Step 1
100mg		100mg	Step 2
100mg	100mg	100mg	Step 3
100mg	100mg	200mg	Step 4
100mg	200mg	200mg	Step 5
200mg	200mg	200mg	Step 6
200mg	200mg	300mg	Step 7
200mg	300mg	300mg	Step 8

Gabapentin - Standard Titration

Morning	Noon	Evening	Duration
		300mg	Step 1
300mg		300mg	Step 2
300mg	300mg	300mg	Step 3
300mg	300mg	600mg	Step 4
300mg	600mg	600mg	Step 5
600mg	600mg	600mg	Step 6

For example: 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 completely stopped, it should be reduced to the lowest effective dose if to be used in the long-term.** Non-pharmacological/self-management options should be highlighted/signposted at all stages.

Other Treatments

Capsaicin Cream 0.075% (Axsain®): Option for localised pain if oral therapy is to be avoided/not tolerated. Apply 3-4 times a day, apply sparingly, not more often than every 4 hours

Pregabalin∞: Schedule 3 CD and not a formulary option. It is not expected to be prescribed routinely. Due to the associated risks, careful consideration must be given before prescribing, and only after formulary choices have been considered and/or tried.

Opioids∞: Neuropathic pain is not particularly responsive to opioids. NICE do not recommend opioids unless under specialist advice.

Tapentadol MR∞: Schedule 2 CD and an opioid. This should only be considered on the recommendation of a specialist

Tramadol∞:Schedule 3 CD and an opioid. NICE recommend tramadol only if acute rescue therapy is needed, and long term only if advised by a specialist.

Lidocaine Plasters: due to limited evidence, NICE does not make a recommendation on the use of lidocaine patches for neuropathic pain.

Carbamazepine: recommended as initial treatment for trigeminal neuralgia. Patients should be monitored accordingly—refer to product SPC.

∞ *In line with legislation, procedures must be in place for regular clinical review/ monitoring of all CDs.*

Note: QT Prolongation. As with many medicines, 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.