NORTHERN IRELAND MEDICINES MANAGEMENT

Health and Social Care Board

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NEWSLETTER

In This Issue

NEW: Deprescribing section

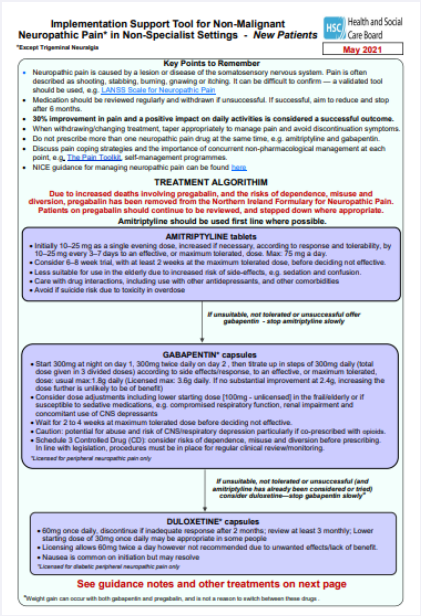
Many national and international guidelines now recognise polypharmacy as a major patient safety issue which needs to be addressed. There is evidence that deprescribing appears to be feasible and generally safe and that medication reviews can reduce inappropriate polypharmacy. To help support deprescribing, this newsletter will include a deprescribing article as a standard topic each month, to focus on specific medicines.

NI Formulary - Pregabalin Removed (Neuropathic Pain)

Between 2013 – 2019, annual deaths in NI where pregabalin was mentioned as being present increased from **1 to 77**. In fact it was the most frequent drug appearing on death certificates in 2019. Together with the risks of dependence, misuse and diversion, this led to the decision to remove pregabalin from the NI Formulary for neuropathic pain. **Patients currently taking pregabalin should continue to be reviewed and stepped down slowly as appropriate**.

Note: Gabapentinoids should not be offered for other types of pain including fibromyalgia, low back pain and sciatica (https://www.nice.org.uk/guidance/ng193/resources/visual-summary-pdf-9073473517).

Refer to the updated Implementation Support Tool for Neuropathic Pain which outlines current NI Formulary choices and guidance. Advice on dose titration and step down is also provided.



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

*Except Trigeminal Neuralgia

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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- Medication should be reviewed regularly and withdrawn if unsuccessful.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 ALGORITHM

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

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

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

Key Points for Managing Neuropathic Pain:

- Ensure neuropathic pain is carefully diagnosed using a validated tool, e.g. LANSS Scale for Neuropathic Pain.
- Amitriptyline is first line choice, gabapentin second line and duloxetine third. Start with a low dose and titrate slowly. Use only one agent at a time.
- Opioids have limited benefit and should **not be prescribed** unless by a specialist. Exception: tramadol for acute rescue therapy only.
- Encourage non-pharmacological strategies throughout treatment.
- 30% pain improvement and improved functioning is considered a success.
- If satisfactory improvement, maintain dose for at least six months. Then reduce **slowly** with a view to stopping **or** maintain at the lowest dose if stopping is not possible.
- Gabapentin (and pregabalin) are Schedule 3 controlled drugs (CD). In line with legislation, procedures must be in place for regular review/monitoring.

Action:

- Follow the NI Formulary choices and guidance for managing neuropathic pain.
- Review patients regularly to assess benefits and adverse effects. For gabapentin (and pregabalin) also check for signs of abuse, misuse or dependence.
- Patients on pregabalin should continue to be reviewed and stepped down slowly as appropriate.
- Do not offer gabapentinoids for other types of pain including fibromyalgia, low back pain or sciatica.

Additional Points to Note:

- **Tapentadol (**Schedule 2 CD, opioid): Specialist advice only
- **Tramadol (**Schedule 3 CD, opioid): Long term use - specialist advice only
- **Lidocaine patches:** Not recommended - limited evidence for use.

Deprescribing: Opioids

Opioids are *high-risk*, useful in acute / palliative situations, but with little evidence for use long-term. A small proportion of people may obtain good analgesia with opioids long-term (estimated 1 in 10) if the dose is kept low and use is intermittent, but they are difficult to identify when starting treatment.

When considering deprescribing, assess if:

- **There is a valid current indication**. If none, investigate.
- **Regular opioids are still needed**. Has underlying condition resolved/been treated, e.g. joint replacement?
- **Opioid is effective**. If pain did not reduce by at least 30% (or other pre-agreed objective, e.g. functional goal, improvement in sleep), then consider opioid ineffective and *discontinue, even if no other treatment is available.* Patients who do not achieve useful pain-relief from opioids within 2-6 weeks* are unlikely to benefit long-term. Continue treatment only if meaningful improvement in pain / function outweighs risks.
- **Patient has intolerable side effects**. Risk (e.g. of falls) can outweigh benefits particularly with weak opioids.
- **There is risk of potentially fatal respiratory depression**. Is there co-prescription with other CNS-depressants?
- **Prescribing is evidence-based**.
  - ◊ Co-codamol, co-dydramol are 'less suitable for prescribing' (i.e. have limited benefit).
  - ◊ Stop: oxycodone/naloxone combination (not cost-effective), co-proxamol (safety issue) and tramadol/ paracetamol combination (no more effective than established analgesics)
  - ◊ Is dose clinically warranted and safe?
- **There is over-ordering**. Check issues over last 6 months. Ensure there is a minimum number of days between prescriptions.
- **There is strong evidence medication is diverted to others**.

* If the patient has constant pain, a trial may be two weeks. If the patient has intermittent disabling flare ups of pain on a background of more manageable symptoms, the trial should be long enough to observe opioids in two or three episodes of increased pain. Opioids Aware notes that if reduction in pain is not achieved following a single dose of immediate relief morphine 20mg, opioids are unlikely to be beneficial in the long term.

Preparation for dose reduction

- Discuss with patient/carers. Agree outcomes. If patient reluctant, consider giving them a self-assessment tool and use the answers to develop discussions.
- Explain
  - ◊ Rationale for stopping: benefits versus long-term harm.
  - ◊ Slow weaning: as withdrawal can cause drug craving, anxiety, insomnia, abdominal pain, vomiting/diarrhoea, diaphoresis, tremor, etc.
  - ◊ Any pain from withdrawal generally passes within 1-2 weeks, lessened by tapering slowly. Plan beforehand how to address this, e.g. non-drug strategies such distraction, stretching, meditation, heat or use of non-opioid medications.

During taper

- Monitor patients for pain, function, and withdrawal.

Refer to GMMMG Opioid Prescribing for Chronic Pain: Resource Pack on Primary Care intranet for further information on how to deprescribe opioids.

NICE GUIDANCE — NI SERVICE NOTIFICATIONS

Service Notifications have been issued in Northern Ireland for the following:

NICE TA617 — Lusutrombopag (Mulpleo, as an option for treating severe thrombocytopenia in adults with chronic liver disease having planned invasive procedures
NICE TA624 — Peginterferon beta-1a (Plegridy) as an option for treating relapsing-remitting multiple sclerosis in adults
NICE TA626 — Avatrombopag (Doptelet) as an option for treating severe thrombocytopenia in adults with chronic liver disease having planned invasive procedures
NICE TA633 — Ustekinumab for treating moderately to severely active Ulcerative Colitis in adults
NICE TA705 — Atezolizumab monotherapy for untreated advanced non-small-cell lung cancer
NICE TA707— Nivolumab for previously treated unresectable advanced or recurrent oesophageal cancer
NICE TA708 — Budesonide orodispersible tablet for inducing remission of eosinophilic oesophagitis
NICE TA709 — Pembrolizumab for untreated metastatic colorectal cancer with high microsatellite instability or mismatch repair deficiency
NICE TA710 — Ravulizumab for treating atypical haemolytic uraemic syndrome

MANAGED ENTRY DECISIONS

No Managed Entry decisions were considered this month.

For previous entries, see Managed Entry section of NI Formulary website.

This newsletter has been produced for GPs and pharmacists by the Regional Pharmacy and Medicines Management Team. If you have any queries or require further information on the contents of this newsletter, please contact one of the Pharmacy Advisors in your local HSCB office:

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