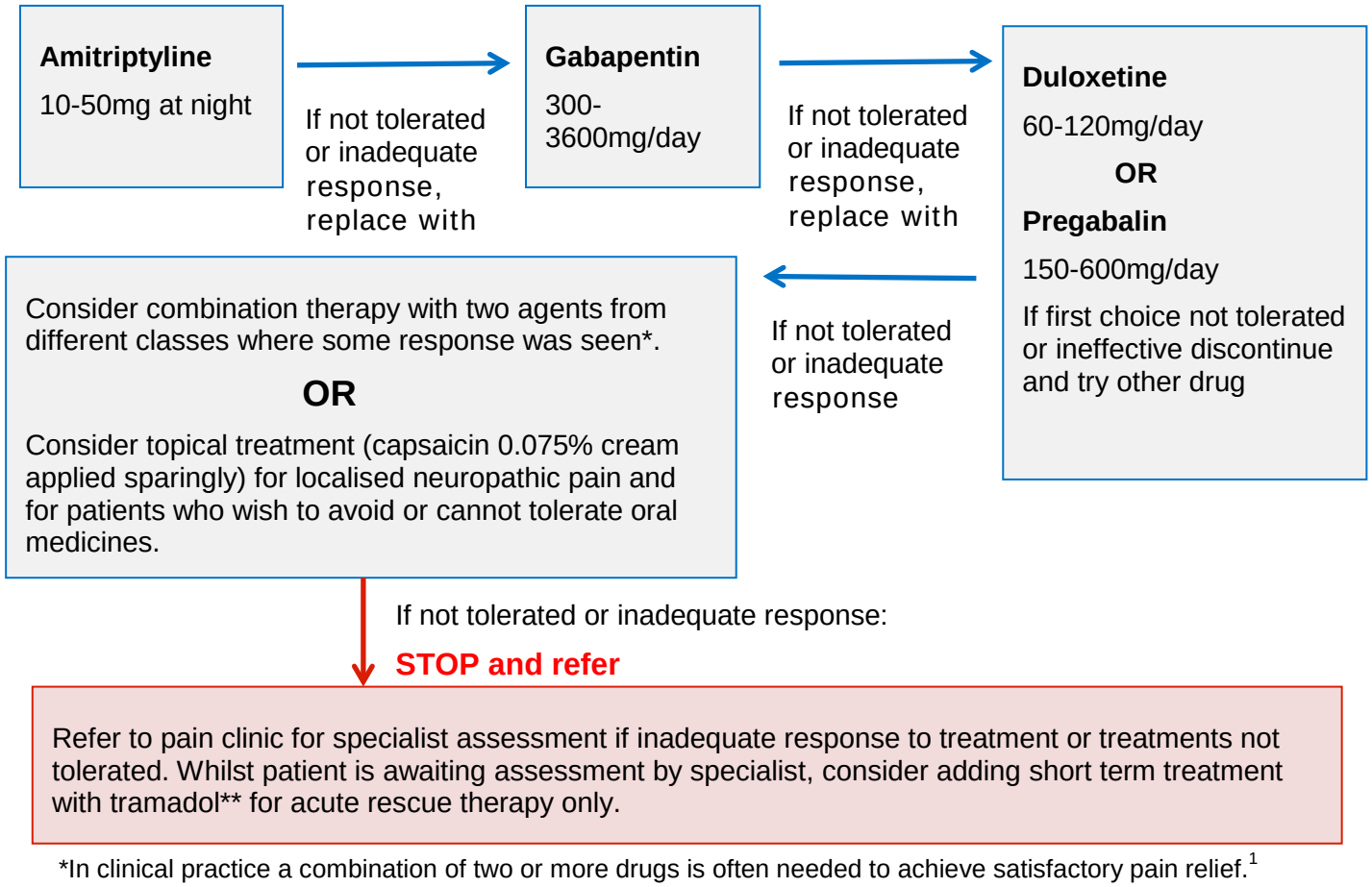
NHS
Northamptonshire
Clinical Commissioning Group

Northamptonshire guidance on the management of neuropathic pain in a non-specialist setting (Adults)

NICE Clinical Guideline 173 advises that amitriptyline, gabapentin, duloxetine or pregabalin may be considered for the first-line treatment of neuropathic pain. This local guidance provides further clarification regarding drug choices and dose titration.

Neuropathic pain algorithm

- If a treatment is not licenced for the prescribed indication ensure the patient understands the unlicensed status of the medicine, and has been given patient information and gives informed consent.
- Consider co-morbidities, side effects and potential for abuse before commencing treatments.
- 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.
- Ongoing review: treatment should be reviewed regularly for continued need. Discontinue repeats for medication no longer being taken.



*In clinical practice a combination of two or more drugs is often needed to achieve satisfactory pain relief.[1] The algorithm reflects this need and proposes that combination therapy is an option before specialist referral. This does not reflect the guidance in the updated NICE Clinical Guideline 173 on neuropathic pain.[2]

** The government has considered concerns raised in relation to tramadol and has decided to place it in Schedule 3 to the Misuse of Drugs Regulations 2001 when it is controlled later in 2014, but with exemption from the safe custody requirements.

Based on NICE CG 173 and the PrescQIPP neuropathic pain template pathway

Approved by NPMG March 2014

DO NOT START THE FOLLOWING TREATMENTS IN NON SPECIALIST SETTINGS

- Capsaicin patch
- Lacosamide
- Lamotrigine
- Levetiracetam
- Morphine
- Oxcarbazepine
- Topiramate
- Tramadol-long term
- Venlafaxine

Lidocaine patches are "double red" in Northamptonshire and will only be approved for the treatment of post-herpetic neuropathic pain with allodynia.

Cannabis Sativa Extract is not commissioned in Northamptonshire and will only be considered via an Individual Funding Request.

Prescribing notes

Many of the treatment options suggested by the NICE Clinical Guideline 173 for neuropathic pain are not licenced for all forms of neuropathic pain but have been used in clinical practice for many years and have an established role in the treatment of neuropathic pain.

NICE CG173 recommends that the GMC good practice in prescribing and managing medicines and devices (2013) guide[3] is followed when treating neuropathic pain

NB Duloxetine is only licensed for diabetic neuropathy; however, the NICE guidance and this local guidance include its (unlicensed) use in non-diabetic neuropathy.

For Trigeminal neuralgia only: Carbamazepine

This is one of several antiepileptics that can be of use for trigeminal neuralgia in addition to the tricyclic antidepressants and gabapentin etc.

Notes[5]

- Initially 100mg (once or divided into twice daily dose) increased gradually according to response. Usual dose 200mg three to four times daily, up to 1.6g total daily dose in some patients.
- If ineffective follow neuropathic pain pathway from step 1.

For all other neuropathic pain

Step 1 – Amitriptyline[4]

Notes[2,5]

- Amitriptyline is unlicensed for use in neuropathic pain but there is a large evidence and practice base to support its use and this is an established indication.
- Typical starting doses are 10mg-25mg at night and should be gradually increased according to the patient's needs. Doses above 50mg are seldom required although up to 75mg may sometimes be tolerated. Pain relief may be seen after 1-7 days but it may take two to six weeks for the drug to be effective.
- Advise patient to take at about 8pm; if morning sedation is problematic the dose may be taken earlier in the evening.

- Particular caution is advised on initiation and after an increase in dose in patients who drive or operate machinery.
- A typical amitriptyline dosage regimen:

  Step 1: - 10mg at night* for 1 week

  Step 2: - 20mg at night* for 1 week then evaluate response

  Step 3: - 30mg at night*

  Step 4: - 40mg at night*

  Step 5: - 50mg at night*

  * Ensure patient tolerates dose at each step before increasing dose.
  After step 2 the dose can be increased gradually according to tolerance and the patient's needs.
- If amitriptyline is not tolerated or is ineffective it should be withdrawn gradually over 1-2 weeks and gabapentin tried.
- http://www.medicines.org.uk/EMC/medicine/23736/SPC/Amitriptyline+Tablets+BP+10mg/

Step 2 –Gabapentin[4]

Notes[2,5]

The anticonvulsant drug of choice is gabapentin (licensed indication for peripheral neuropathy, not licenced for central neuropathy). Capsules are the most cost-effective formulation.

NB. 2 x 400mg capsules are considerably less expensive than 1x 800mg tablets.

Gabapentin should be started slowly according to the regimen below. In renal impairment, the elderly or drug sensitive patients, this titration may need to be done in 100mg increments. Refer to the SPC for more details. Slower titration and particular caution is advised on initiation and after an increase in dose in patients who drive or operate machinery.

http://www.medicines.org.uk/emc/medicine/25430/SPC/Gabapentin+100+mg+Capsules/

A typical dosage regimen for gabapentin[6]

For neuropathic pain dose range is 900mg to 3600mg daily (dose reduced in renal impairment). Treatment can be initiated at a dose of 900mg/day given as three equally divided doses or at a slower rate as described below:

Step 1: Gabapentin 300mg once daily on day 1.
Step 2: Gabapentin 300mg twice daily on day 2.
Step 3: Gabapentin 300mg three times daily on day 3.

Slower titration of gabapentin may be appropriate for individual patients to improve tolerability.

Once a patient is on a 900mg dose, the dose can be increased in 300mg increments every two to three days until tolerated. The dose should be increased to either the dose that provides sufficient pain relief or the maximum tolerated dose. The maximum daily dose is 3600mg, however in practice many patients do not go over a dose of 1800mg.

An example of a dose increase regimen is shown below:

Step 4: Gabapentin 300mg morning and 300mg mid-day + 600mg night until tolerated.*
Step 5: Gabapentin 600mg morning and night and 300mg mid-day until tolerated.*
Step 6: Gabapentin 600mg morning, 600mg mid-day and 600mg night until tolerated.*

*Usually 2-3 days but may take up to a week in some patients.

The minimum time to reach a dose of 1800 mg/day is one week, to reach 2400 mg/day is a total of 2 weeks, and to reach 3600 mg/day is a total of 3 weeks.

- Side effects are usually minor and subside within 4 weeks.
- Gabapentin can make patients drowsy or dizzy and occasionally causes severe headaches. Severe headaches do not tend to resolve, treatment should be reduced gradually. Serious adverse effects are rare.

If there is no improvement within 8 weeks of reaching the maximum tolerated therapeutic dose, consider alternative treatment. Gabapentin should not be stopped abruptly and should be reduced gradually over a minimum of 1 week, depending on dose and duration of treatment.

In the treatment of peripheral neuropathic pain such as painful diabetic neuropathy and post-herpetic neuralgia, efficacy and safety have not been examined in clinical studies for treatment periods longer than 5 months. If a patient requires dosing longer than 5 months for the treatment of peripheral neuropathic pain, the treating physician should assess the patient's clinical status and determine the need for additional therapy.

Step 3: Duloxetine or Pregabalin

Duloxetine

This can be considered a third line treatment for neuropathic pain (licenced for the treatment of diabetic neuropathy only) in patients who have not achieved adequate pain relief from, or who have not tolerated, first and second line treatments i.e. with amitriptyline or gabapentin. [5,4] In prisons and other secure environments duloxetine is recommended for consideration prior to prescribing gabapentin or pregabalin due to the risk of abuse and diversion of these medicines.[7]

- The dose is 60mg once daily, increased to a maximum of 120mg daily in divided doses.
- Treatment should be discontinued after 8 weeks if there is an inadequate response.

Treatment should be reviewed at least every three months for continued need.

Pregabalin

Pregabalin is a pro-drug of gabapentin and is an alternative to gabapentin in patients who have not achieved adequate pain relief from, or have not tolerated, first and second line treatments. This drug can be used in combination with a tricyclic anti-depressant, but it should not be co-prescribed with gabapentin (note there may be some crossover when titrating treatments at change of therapy). Cases of abuse have been reported. Caution should be exercised in patients with a history of substance abuse and the patient should be monitored for symptoms of pregabalin abuse.

- Pregabalin is licensed for neuropathic pain.
- Pregabalin should be started slowly and titrated to response and tolerability as detailed below.
- The dose must be reduced in renal impairment and may need to be reduced in older people, or drug sensitive patients.
- Dosing should be twice daily as this is considerably less expensive than three times a day dosing.
- Pregabalin can make patients drowsy or dizzy and may cause confusion.

Dose range is 150mg to 600mg daily (reduce dose in renal impairment).

A typical dose regimen for pregabalin:[8]

Pregabalin 75mg morning and night until tolerated (usually 3 to 7 days), if a dose increase is needed use

Pregabalin 150mg morning and night until tolerated (after 7 days), if a further dose increase is needed use

Pregabalin 300mg morning and night until tolerated- no further dose increase is recommended as 600mg daily is the maximum dose.

The starting dose may need to be reduced in drug sensitive or elderly patients. A suitable starting dose may be 25mg twice daily (morning and night). This should be titrated slowly to response and tolerability. Slower titration and particular caution is advised on initiation and after an increase in dose in patients who drive or operate machinery.

Dosage reduction is required in patients with compromised renal function. Refer to the SPC for details.

Pregabalin should be stopped if the patient has not shown sufficient benefit within 8 weeks of reaching the maximum tolerated therapeutic dose and referred to the Pain Clinic. It should not be stopped abruptly but should be reduced gradually over a minimum of 1 week.

Review long term use and assess the need to continue treatment.

References

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