# Neuropathic Pain – Primary Care Pharmacological Management

## Neuropathic Pain Pathway for Adults in Primary Care

### Trigeminal neuralgia – Carbamazepine first line
- Start 100mg od- bd increasing to an effective or maximum tolerated dose
- Aim for 400mg m/r bd (maximum 1.6g / day )
- When pain relief obtained, try to gradually discontinue therapy, until another attack occurs
- If not effective, not tolerated or contraindicated consider seeking specialist advice or follow pain pathway below

### All Neuropathic Pain (except trigeminal neuralgia)

#### Step 1
- Amitriptyline (where no cautions or contraindications)
  - Start 10mg 6-8pm to reduce ‘hangover’ effect
  - Increase gradually by 10mg/week to an effective or maximum tolerated dose
  - Aim for at least 25mg nocte (not above 75mg)
  - Inadequate response after 8 week trial or not tolerated discontinue

#### Step 2
- Gabapentin (capsules are more cost effective)
  - Start: Day 1: 300mg  Day 2: 300mg bd  Day 3: 300mg tds
  - Increase gradually in 300mg/day increments every 2-3 days to an effective or maximum tolerated dose
  - Aim for at least 600mg tds (maximum 1.2g tds)
  - Allow 1 week to reach 1.2g/day, 2 weeks for 2.4g/day and 3 weeks for 3.6g/day
  - If tolerability an issue titrate using 100mg capsules:
    - Start 100mg tds x1week, 200mg tds x1 week, then 300mg tds
  - Inadequate response after 8 week trial or not tolerated discontinue

#### Step 3
- Duloxetine
  - Start 60mg od (maintenance dose), up to maximum 60mg bd (no evidence at higher dose)  OR
- Pregabalin
  - Start 75mg bd. Increase if necessary after 3-7 days to 150mg bd, then after further 7 days to maximum 300mg bd
  - If tolerability an issue start 25mg bd, increase after 1-2 weeks to 50mg bd
  - Prescribe as bd dose (no benefit in tds) and AVOID double dosing e.g. 2bd

If first choice is not tolerated or inadequate response after 8 week trial – discontinue and try other drug

#### Topical treatment
- Consider capsaicin cream for people with localised neuropathic pain who wish to avoid, or who cannot tolerate oral treatments

### STOP AND REFER TO PAIN CLINIC
- Consider referral to specialist setting at any time if: pain is severe or significantly limits lifestyle, daily activities and participation, their underlying health condition has deteriorated, or their pain has not responded to above medication (include medicines and doses previously tried in referral letter)
- Consider adding tramadol only for acute rescue therapy prior to assessment by specialist

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*This is local opinion in consultation with Dr Oliver Hart, Feb 2014*
Introduction

This guidance is to assist general practitioners with the pharmacological management of neuropathic pain, including trigeminal neuralgia. It is based on the updated NICE Clinical Guideline 173: Neuropathic pain – pharmacological management; and offers a suggested algorithm for treatment and general prescribing advice.

Diagnosing neuropathic pain

Neuropathic pain is defined by the International Association for the Study of Pain (IASP 2011) as ‘pain caused by a lesion or disease of the somatosensory nervous system’. It is often difficult to diagnose and treat because of the heterogeneity of its aetiologies, symptoms and underlying mechanisms.

- Can be intermittent or constant, and spontaneous or provoked.
- Encourage patients to describe their pain. Trigger words include: shooting, stabbing, like an electric shock, burning, tingling, tight, numb, prickling, itching and a sensation of pins and needles.
- There are many possible causes.
- Screening tools: Appendix 1: DN4 questionnaire and Appendix 2: S-LANSS questionnaire may be helpful in diagnosing neuropathic pain and in establishing an initial baseline before starting treatment.

Initiation, Dose titration and Clinical review

- Success of pharmacological therapy is likely to be reduction in pain and not elimination - clinical trials frequently use 30-50% pain relief as an end point.
- Set realistic goals for pain relief by pharmacological therapy - remember these drugs will work well in some patients, moderately in others and for some there will be no benefit.

Initiation

- Consider co-morbidities, side effects and potential for abuse before starting therapy:
  - Amitriptyline, gabapentin and pregabalin can all cause dizziness and drowsiness: particular caution is required when starting therapy and after a dose increase in patients who drive or operate machinery.
  - Continue simple analgesia where there is evidence of pain relief.
  - If a treatment is not licensed for the prescribed indication, ensure patient understands and gives informed consent.
  - For more detailed information on a particular drug, for example: contraindications, cautions, side effects go to the SPC (Summary of Product Characteristics) - www.medicines.org.uk

Dose titration

- The pain pathway advocates slow titration to minimise side effects. Whilst this is helpful in those with chronic pain, a more rapid titration may be appropriate for acute severe pain such as sciatica.
- Some patients may need lower doses and slower titration to minimise side effects.
- Aim for an effective or maximum tolerated dose. Ensure current dose is tolerated before increasing further.
- There may be some cross over with treatments as one is ‘stepped down’ and the other started.
Clinical reviews

- Ask patients to keep a diary. Appendix 3: Neuropathic Pain Patient Record
- **After starting or changing a treatment, carry out an early clinical review (2 weeks)** to assess dosage titration, tolerability, adverse effects and suitability of chosen treatment.
- **Review after 8 weeks**, or once the dose is titrated to an adequate dose (if longer). Additional benefit is unlikely after 8 weeks. Discontinue drug if inadequate response (reduce dose slowly over at least 1-2 weeks).
- **Carry out regular clinical reviews** to assess and monitor effectiveness of the treatment including: pain control; impact on lifestyle, daily activities (including sleep disturbance) and participation; physical and psychological wellbeing (including anxiety); adverse effects; and continued need for treatment.
- **For treatments that are effective continue for 6 months then consider dosage reduction** and trial withdrawal to assess continued benefit. If pain recurs re-start treatment or if condition resolves step down treatment.

Misuse of pregabalin and gabapentin

- Both gabapentin and pregabalin have: potential to be abused (particularly when prescribed with opiates), known psychiatric side effects including euphoria and hallucinations and a ‘high street value’.
- Ensure careful consideration is given before pregabalin or gabapentin are prescribed to patients with a history of substance misuse or those that have recently been released from prison and review treatment regularly.

Prescribing notes

**Step 1 - Amitriptyline (tricyclic antidepressant)**
- Unlicensed in neuropathic pain but there is a large evidence and practice base to support its use and this is an established indication.
- Pain relief may be seen after 1-7 days but it may take 2-6 weeks to be effective.
- Side effects: sedation may be a problem for some patients but helpful in others; elderly more susceptible to side effects. If 10mg not tolerated after 1-2 weeks consider halving tablet.
- Contraindications include: severe liver disease, recent history of MI, arrhythmias (particularly heart block).
- No dosage adjustment required in renal impairment.

**Step 2 - Gabapentin (anticonvulsant)**
- Licensed for peripheral neuropathic pain.
- Side effects are usually minor and subside within 4 weeks (exception is severe headache).
- Renal impairment requires a lower total daily dose.
- Titrate in 100mg increments in renal impairment, elderly or drug sensitive patients.

**FACTORS TO CONSIDER BEFORE MOVING TO STEP 3**

**Combination of amitriptyline and gabapentin**
- NICE Clinical Guideline 173 did not include advice on combination therapy but it acknowledged that in practice it may be more practical and effective than switching to another treatment in some patients.

**Step 3 - Duloxetine or Pregabalin: see notes overleaf**
Step 3 continued:

**Duloxetine (SNRI)**
- Licensed for diabetic neuropathy only (evidence is only with 60mg od not 120mg od). Also licensed for major depressive disorder and generalised anxiety.
- Consider this particularly if patients have diabetic neuropathy, depression as a prominent co-morbidity (which is not currently being treated) or they have had a poor response to gabapentin.
- It may be a useful alternative to gabapentin and pregabalin if there are concerns over misuse.
- Contraindications include: uncontrolled hypertension, liver disease resulting in hepatic impairment, CrCl < 30ml/min (BNF advises avoid if eGFR < 30mL/min/1.73m²).

**Pregabalin (anticonvulsant)**
- Licensed for peripheral and central neuropathic pain.
- Pregabalin’s mode of action at reducing pain is similar to gabapentin’s – it may therefore be a helpful alternative to gabapentin when there has been some response with gabapentin but dose titration is limited by side effects.
- Pregabalin seems to be particularly helpful if anxiety is a prominent co-morbidity or as with some chronic patients it may help the emotional overload when there is a flare up in their condition.
- Side effects include: drowsiness, dizziness and confusion.
- Renal impairment - Lower starting dose and total daily dose.
- Review progress at 4-8 weeks. Consider benefits in sleep and anxiety as well as pain relief.

**Trigeminal neuralgia - carbamazepine**
- Licensed for paroxysmal pain of trigeminal neuralgia.
- Contraindications include: AV conduction abnormalities, history of bone marrow depression or acute porphyria; or in combination with monoamine oxidase inhibitors (MAOIs).
- Patients and their carers must be advised on how to recognise signs of blood, liver and skin disorders. Medical advice must be sought if symptoms such as fever, sore throat, rash, mouth ulcers, bruising or bleeding develop.

**Do not start the following in non-specialist settings:** morphine, tramadol long-term, oxcarbazepine, topiramate, venlafaxine, lacosamide, lamotrigine, levetiracetam, cannabis sativa extract, capsaicin patch

**Palliative patients** –see [Sheffield Palliative Care Formulary](http://www.prescqipp.info/)

**References**

Guideline prepared by: Helen Taylor, Medicines Management Pharmacist, Sheffield CCG
Input from: Dr Ollie Hart, GPwSI Pain and Dr Richard Oliver
Consultation with Sheffield Teaching Hospitals

Date Approved by Area Prescribing Group: April 2014 Review date: April 2017
Appendix 1: DN4 Neuropathic Pain Assessment Questionnaire

DN4 stands for Douleur Neuropathique 4

<table>
<thead>
<tr>
<th>Patient assessment: Please tick the box that best describes the pain you have at present. Please give to your doctor or nurse when completed</th>
<th>Yes</th>
<th>No</th>
</tr>
</thead>
<tbody>
<tr>
<td>Question 1: Does the pain have one or more of the following characteristics?</td>
<td></td>
<td></td>
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<tr>
<td>Burning</td>
<td>□</td>
<td>□</td>
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<td>Painful cold</td>
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<td>□</td>
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<td>Electric shocks</td>
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<tr>
<td>Question 2: Is the pain associated with one or more of the following symptoms in the same area?</td>
<td></td>
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<tr>
<td>Tingling</td>
<td>□</td>
<td>□</td>
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<tr>
<td>Pins and needles</td>
<td>□</td>
<td>□</td>
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<tr>
<td>Numbness</td>
<td>□</td>
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<tr>
<td>Itching</td>
<td>□</td>
<td>□</td>
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<table>
<thead>
<tr>
<th>Clinician assessment using pin, touch and brush</th>
<th>Yes</th>
<th>No</th>
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<tbody>
<tr>
<td>Question 3: Is the pain located in an area where the physical examination reveals one or more of the following characteristics?</td>
<td></td>
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<tr>
<td>Hypoaesthesia to touch (reduced sensation)</td>
<td>□</td>
<td>□</td>
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<tr>
<td>Hypoaesthesia to pin prick (reduced sensation)</td>
<td>□</td>
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<tr>
<td>Question 4: In the painful area, can the pain be caused or increased by: Brushing (with a brush or cotton wool)</td>
<td>□</td>
<td>□</td>
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</tbody>
</table>

Score total: [ ]

Yes = 1, No = 0 Score > than 4 is likely to be diagnostic of neuropathic pain
Appendix 2: S-LANSS Neuropathic Pain Assessment Questionnaire

THE S-LANSS PAIN SCORE

NAME________________________ DATE______________________

- This questionnaire can tell us about the type of pain that you may be experiencing. This can help in deciding how best to treat it.

- Please draw on the diagram below where you feel your pain. If you have pain in more than one area, only shade in the one main area where your worst pain is.

![Diagram of a human figure with areas shaded]

- On the scale below, please indicate how bad your pain (that you have shown on the above diagram) has been in the last week where: '0' means no pain and '10' means pain as severe as it could be.

NONE 0 1 2 3 4 5 6 7 8 9 10 SEVERE PAIN

- On the other side of the page are 7 questions about your pain (the one in the diagram).

- Think about how your pain that you showed in the diagram has felt over the last week. Please circle the descriptions that best match your pain. These descriptions may, or may not, match your pain no matter how severe it feels.

- Only circle the responses that describe your pain. Please turn over.
Appendix 2: S-LANSS Neuropathic Pain Assessment Questionnaire

**S-LANSS**

1. In the area where you have pain, do you also have ‘pins and needles’, tingling or prickling sensations?
   a) NO - I don't get these sensations (0)
   b) YES - I get these sensations often (5)

2. Does the painful area change colour (perhaps looks mottled or more red) when the pain is particularly bad?
   a) NO - The pain does not affect the colour of my skin (0)
   b) YES - I have noticed that the pain does make my skin look different from normal (5)

3. Does your pain make the affected skin abnormally sensitive to touch? Getting unpleasant sensations or pain when lightly stroking the skin might describe this.
   a) NO - The pain does not make my skin in that area abnormally sensitive to touch (0)
   b) YES - My skin in that area is particularly sensitive to touch (3)

4. Does your pain come on suddenly and in bursts for no apparent reason when you are completely still? Words like ‘electric shocks’, jumping and bursting might describe this.
   a) NO - My pain doesn’t really feel like this (0)
   b) YES - I get these sensations often (2)

5. In the area where you have pain, does your skin feel unusually hot like a burning pain?
   a) NO - I don’t have burning pain (0)
   b) YES - I get burning pain often (1)

6. Gently rub the painful area with your index finger and then rub a non-painful area (for example, an area of skin further away or on the opposite side from the painful area). How does this rubbing feel in the painful area?
   a) The painful area feels no different from the non-painful area (0)
   b) I feel discomfort, like pins and needles, tingling or burning in the painful area that is different from the non-painful area (5)

7. Gently press on the painful area with your finger tip then gently press in the same way onto a non-painful area (the same non-painful area that you chose in the last question). How does this feel in the painful area?
   a) The painful area does not feel different from the non-painful area (0)
   b) I feel numbness or tenderness in the painful area that is different from the non-painful area (3)

**Scoring:** a score of 12 or more suggests pain of predominantly neuropathic origin
Appendix 3: Patient record. Documenting how you are feeling each day will help show whether your treatment is suiting you or not. Remember to bring this with you to future appointments

<table>
<thead>
<tr>
<th>Start date:</th>
<th>Day 1</th>
<th>Day 2</th>
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<td>Has your pain improved?</td>
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<td>How is your general mood? How do you feel in yourself generally?</td>
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<td>How are you sleeping?</td>
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<td>Have you been able to do any of the things that you had stopped doing because of your pain? For example: jobs around the house, work, driving, social activities, exercise &amp; activity</td>
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<td>Have you had any problems with your medication?</td>
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<td>Have you experienced any side effects from your medication?</td>
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