GUIDELINE FOR NON-SPECIALISTS TREATING PATIENTS WITH NEUROPATHIC PAIN

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medicines.info@uhl-tr.nhs.uk
Introduction and purpose

This guideline is intended to be used within the Leicestershire health community to offer guidance to general practitioners in treating patients with neuropathic pain, including trigeminal neuralgia & post-herpetic neuralgia. It offers suggested algorithms for treatment & assessment of patients, and guides when patients need to be referred into secondary care to the chronic pain service. Primary care remains responsible for the diagnosis, treatment, prescribing of medication and monitoring of their patient until they are referred to secondary care.

Disease Background

Neuropathic pain is a very common problem in many neurological diseases and is estimated to affect up to 1.5% of the population. The International Association for the Study of Pain (IASP) 1994 definition of neuropathic pain has been updated by the Neuropathic Pain Working Group 2006 as ‘Pain arising as a direct consequence of a lesion or disease affecting the somatosensory system’. Neuropathic pain includes postherpetic neuralgia which is associated with the herpes zoster infection and is defined as pain that persists for >120 days after the onset of rash. Trigeminal neuralgia is also caused by dysfunction of neural tissue but its treatment is distinctive from the other forms. It is classified as a severe unilateral paroxysmal facial pain in the distribution of the trigeminal nerve.

Pharmacological Interventions

Neuropathic pain can be treated by unconventional analgesics e.g. antidepressants, anticonvulsants as well as conventional medications such as opioids. Some unconventional analgesics e.g. tricyclic antidepressants are used outside their normal licensed indications.

The starting dose and any titration of each pharmacological intervention should be planned, taking into consideration the potential side-effects and interactions with other medication that the patient may be taking. This remains the responsibility of the General Practitioner.

For full prescribing information of pharmacological agents, see the most recent copy of the British National Formulary (BNF) or consult the Summary of Product specification (SPC).

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NEUROPATHIC PAIN

SYMPTOMS

1. Pins and needles, pricking or tingling
2. Abnormally sensitive skin, itch, tight/stretch/squeezing sensations
3. Pain jumps, Shock-like, shoots, stabs
4. Pain is burning, cold or numb

SIGNS

Allodynia
Hyperalgesia
Dysaesthesia
Paraesthesia
Hyperaesthesia
Hypoalgesia
Anaesthesia
Swelling
Colour change
Change in sweating of limb

Check:
- Fasting glucose, FBC, U & E's
- LFT's, B12, Folate, TFT's, CRP
- Bone analysis (Calcium)
- Alcohol intake
- Medication/drug intake
- Family history
- Urinalysis (protein/glucose/blood)
- HIV (if clinically indicated)
- Rash (vasculitic)

If indicated possible drug advice from the Pain clinic would be:
1. Antidepressant group (Amitriptyline up to 75 mg daily, Nortriptyline up to 75 mg daily or Duloxetine 60 mg daily [30mg 1st week] side effects permitting)
2. Antiepileptic group (Gabapentin** up to 1.8 g daily or Pregabalin 75 mg b.d increase to 300 mg b.d. [renal dysfunction 25 mg b.d.])
** local advice is to titrate gabapentin slowly to reduce side effects e.g. 100mg bd, 200mg bd, 300mg tds, 400mg tds at one week intervals, or two day intervals for inpatients.
2. Focal neuropathy (not PHN): a. Lidocaine 5% plaster when other treatment has failed or is contraindicated (expect at least 30% relief)
   b. Capsaicin cream 0.025%-0.075%
3. Tramadol short term use only for breakthrough pain relief maximum dose 400 mg daily. Beware of interactions (serotonin syndrome) with tricyclic antidepressant / SSRI. Care in the elderly.
4. Other Opioids should NOT be used except under the guidance of the pain clinic (e.g. morphine, oxycodone, tapentadol SR)
   Prescribers should be fully aware of drug pharmacology, side effects and interactions.

Opiates for neuropathic pain are not always effective. Beware of rapid dose escalations. Patients often require psychological support. Please refer to the document opiates for non malignant pain. The British Pain Society.

Designed by UHL Pain Service in conjunction with Local GP's
TRIGEMINAL NEURALGIA

Severe unilateral intermittent lancinating facial pain
Pain triggered by known trigger factors e.g. wind, cold, shaving, cleaning teeth.
Patient or doctor demonstrates trigger zones

Check for neurological symptoms or signs?

Scan abnormal

Refer to Neurology or neurosurgery

MRI referral must state 'UHL trigeminal neuralgia pathway', if neurological symptoms present, if considering vascular loop in cerebellomedullary angle or if MS is suspected.

Scan normal

Obtain neurosurgical opinion; if surgery not an option then it is probably idiopathic trigeminal neuralgia

Has treatment been effective?

No

Refer to Pain Service

Drugs used in the treatment plan may include the following

First line: carbamazepine up to 1.2 g daily
Second line:
Gabapentin up to 1.2-1.8g daily titrating over several weeks
Pregabalin up to 300mg b.d.

IF INEFFECTIVE AT ADEQUATE DOSAGE OR IN COMBINATION, DRUGS SHOULD BE STOPPED.

Pain Service may recommend: Oxcarbazepine
up to 300mg b.d. initially (unlicensed)
Lamotrigine up to 100 mg b.d. (unlicensed)
## POST HERPETIC NEURALGIA

Typical history of prodrome and rash in a dermatomal distribution

Shooting/burning pain in the same area as the rash. Allodynia (pain following an innocuous stimulus)

<table>
<thead>
<tr>
<th>YES</th>
<th>NO</th>
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**Patient less than 60 years**

### Drugs used in treatment plan may include the following in recommended order:

1. Lidocaine Plaster 5% up to 3 plasters daily
2. Tricyclic Antidepressant eg Amitriptyline, Nortriptyline 10-100mg daily depending on age (unless contraindicated or not tolerated)
3. Duloxetine 60 mg daily (30 mg 1st week) side effects permitting
4. Gabapentin up to 1.2 g - 1.8 g daily using titration over several weeks
5. Pregabalin up to 300mg bd if Gabapentin ineffective or not tolerated
6. Tramadol up to 100mg qds short term use only. Beware of interactions (serotonin syndrome) with tricyclic antidepressant / SSRI.
7. Capsaicin cream 0.075% qds

**ALL TO BE TRIED FOR 3 MONTHS; SIDE EFFECTS PERMITTING.** If ineffective at adequate dosage or in combination, drugs should be stopped.

**Prescribers should be fully aware of drug pharmacology, side effects and interactions.**

**Patient over 60 years or cardiovascular problems**

### Drugs used in the treatment plan may include the following in recommended order:

1. Lidocaine Plaster 5% up to 3 plasters daily
2. Gabapentin up to 1.2 g - 1.8 g daily using titration over several weeks
3. Pregabalin up to 300mg bd if Gabapentin not tolerated or effective
4. Duloxetine 60 mg daily (30 mg 1st week)
5. Tricyclic Antidepressant eg Amitriptyline, Nortriptyline 5-100mg daily depending on age (care in the elderly) unless contraindicated
6. Tramadol up to 100mg qds short term use only. Beware of interactions (serotonin syndrome) with tricyclic antidepressant / SSRI.
7. Capsaicin cream 0.075% qds

**ALL TO BE TRIED FOR 3 MONTHS; SIDE EFFECTS PERMITTING.** If ineffective at adequate dosage or in combination, drugs should be stopped.

**HAVE THESE TREATMENTS BEEN EFFECTIVE?**

- **Yes:** Refer to pain service
- **No:** Further treatment options may need to be considered
<table>
<thead>
<tr>
<th>Drug</th>
<th>Dose and route</th>
<th>Maximum daily dose</th>
<th>Dose titration &amp; duration of trial</th>
<th>Side-effects/comments</th>
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<tbody>
<tr>
<td><strong>Tricyclic antidepressants</strong></td>
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<tr>
<td>Amitriptyline (unlicensed)</td>
<td>89p 10mg $£43.00 x 28</td>
<td>Up to 75mg daily (higher doses under specialist supervision of 150mg dependent on age &amp; comorbidity)</td>
<td>Increase dose by 10 to 25mg weekly. Duration of adequate trial 3 months at maximum tolerated dosage</td>
<td>Side-effects: Dry mouth, sedation, cardiotoxicity, postural hypotension, bladder problems, constipation. Give dose at night to minimise sedation. Unlicensed indication.</td>
</tr>
<tr>
<td>Nortriptyline (unlicensed)</td>
<td>£84.48 x 100 25mg</td>
<td>Up to 75mg daily (higher doses under specialist supervision, see above)</td>
<td>Increase dose by 10 to 25mg weekly. Duration of adequate trial 3 months at maximum tolerated dosage</td>
<td>Use in place of amitriptyline if sedation with amitriptyline is problematic. Unlicensed indication.</td>
</tr>
<tr>
<td><strong>Anti-epileptics</strong></td>
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<td>Gabapentin</td>
<td>£4.49 x 100 300mg caps 300mg</td>
<td>Maximum dose 1.8g daily in 3 divided doses.</td>
<td>Increase dose gradually each week to a max of 1.8g total daily dose. Duration of adequate trial 3 months in total including titration period.</td>
<td>Side-effects: Dry mouth, dizziness and cognitive impairment. Licensed for treatment of neuropathic pain (age &gt;18 years), unlicensed use in trigeminal neuralgia.</td>
</tr>
<tr>
<td>Pregabalin</td>
<td>£64.40 x 56 75mg</td>
<td>Maximum dose 600mg daily in 2 divided doses</td>
<td>Increase after 3-7 days to 150mg BD, increased further if necessary after 7 days to maximum dose of 300mg BD. 3 month trial to assess efficacy.</td>
<td>Licensed for treatment peripheral and central neuropathic pain (age &gt; 18 years) <strong>Consider if side effects develop with gabapentin, which aren't tolerated but has a response to therapy</strong> (these could also be a problem with pregabalin).</td>
</tr>
<tr>
<td>Carbamazepine (Trigeminal neuralgia only)</td>
<td>£16.32 x 84 200mg</td>
<td>Maximum 1.6g daily in some patients given in divided doses.</td>
<td>Small doses should be used initially to minimise side-effects. Build up dose slowly with increments of 200mg every week. 3 month trial to assess efficacy.</td>
<td>Licensed for treatment of paroxysmal pain of trigeminal neuralgia. Counsel patient to recognise signs of blood, hepatic or skin disorders – seek medical advice if fever, sore throat, rash or mouth ulcers, bruising/bleeding develop. Side effects; dizziness, nausea &amp; vomiting, visual disturbances.</td>
</tr>
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</table>

**Table 1: Medicine Information on Pharmacological Agents for Neuropathic Pain**
<table>
<thead>
<tr>
<th>Drug</th>
<th>Dose and route</th>
<th>Maximum daily dose</th>
<th>Dose titration &amp; duration of trial</th>
<th>Side-effects/comments</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Oxcarbazepine (trigeminal neuralgia [unlicensed indication])</strong> £45.65 x 50 600mg</td>
<td>Initially 300 mg twice daily increased according to response in steps of up to 600 mg daily at weekly intervals; usual dose range 600mg –2.4g daily in divided doses</td>
<td>Maximum 2.4g daily in some patients given in divided doses.</td>
<td>Small doses should be used initially to minimise side-effects. Build up dose slowly with increments up to 600mg every week. 3 month trial to assess efficacy.</td>
<td>Counsel patient to recognise signs of blood, hepatic or skin disorders – seek medical advice if fever, sore throat, rash or mouth ulcers, bruising/bleeding develop. Side effects; dizziness, nausea &amp; vomiting, visual disturbances.</td>
</tr>
<tr>
<td><strong>Lamotrigine (unlicensed)</strong> £1.49 x 56 25mg</td>
<td>Initially 25mg daily orally for 2 weeks, increased to 50mg daily for 2 weeks</td>
<td>Titrated upwards every 7 days by 50-100mg until reach maximum of 100mg BD</td>
<td>Titrate slowly to minimise side effects. 3 month trial to assess efficacy including titration period.</td>
<td>Counsel patients to contact doctor if signs of rash, most occur within first 8 weeks of therapy. Be alert also for signs of bone marrow suppression e.g. anaemia, bruising or infection.</td>
</tr>
<tr>
<td><strong>Serotonin &amp; noradrenaline re-uptake inhibitor anti-depressants</strong></td>
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<tr>
<td><strong>Duloxetine (Cymbalta®) £27.72 x 28 60mg</strong></td>
<td>Initially 30mg for one week (to minimise side effects including nausea)</td>
<td>Maximum 60mg daily</td>
<td>Titrate to 60mg OD after first week. Trial period to assess efficacy <strong>2 months.</strong></td>
<td>Licensed for diabetic neuropathy in &gt;18 years of age. Side effects; drowsiness, constipation, dry mouth, insomnia, nausea.</td>
</tr>
<tr>
<td><strong>Additional therapy</strong></td>
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<tr>
<td><strong>Lidocaine (Versatis®) £72.40 x 30 5%</strong></td>
<td>5% w/w medicated plaster for topical application. Plaster to be applied to affected area for up to 12 hour duration. Plaster-free period of at least 12 hours a day. Up to 3 plasters may be used to cover large areas; plasters may be cut</td>
<td>A maximum of 3 plasters to be applied once daily for up to 12 hours, at any one time to cover the affected area.</td>
<td>Some pain relief may occur on 1st day of using the plaster. It may take up to 2-4 weeks until the full pain-relief effect is seen. Trial period to assess efficacy <strong>1 month.</strong></td>
<td>Lidocaine 5% medicated plaster is licensed for treatment of pain caused by post-herpetic neuralgia. Useful in the elderly population as topical application minimises side effect profile. Side-effects: skin irritation at or around site of application.</td>
</tr>
<tr>
<td><strong>Capsaicin cream (Axsain®) £14.58 x 45g</strong></td>
<td>Capsaicin 0.075% topical cream. Apply a small amount up to 3-4 times a day</td>
<td>Do not apply more than four times a day.</td>
<td>Trial period to assess efficacy <strong>2 months.</strong></td>
<td>Avoid contact with eyes, inflamed &amp; broken skin. Only to be used for postherpetic neuralgia once open skin lesions have healed. Hands should be washed immediately after use. Side effects include transient burning sensation during initial treatment.</td>
</tr>
</tbody>
</table>
### Drug, Dose and route, Maximum daily dose, Dose titration & duration of trial, Side-effects/comments

<table>
<thead>
<tr>
<th>Drug</th>
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</thead>
<tbody>
<tr>
<td>Baclofen (unlicensed) £1.75 x 84 10mg</td>
<td>Initially 10mg OD, orally with or after food. Increased after 7 days if necessary to 10mg BD for 7 days then 10mg TDS</td>
<td>Maximum dose 30mg TDS</td>
<td>Titrate slowly each week to minimise side effects. 3 month trial period to assess efficacy.</td>
<td>Side effects include sedation, nausea, urinary disturbances, ataxia, insomnia, hallucinations.</td>
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**Duration of trial:**

If partial response occurs to 1st drug, consider adding in another drug from a different class. If no response is seen within the trial period or side effects are intolerable discontinue therapy and choose another agent from the treatment algorithm.

**Chronic Pain Contact at UHL & referral system:**

Chronic Pain Service at UHL can be contacted on telephone 0116 258 5653
Any referrals into the hospital should be completed through the “choose & book” system available at your surgery.
References


Drug Tariff January 2014


Glossary of Terms:

<table>
<thead>
<tr>
<th>SYMPTOM</th>
<th>DEFINITION</th>
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<tbody>
<tr>
<td>ALLODYNIA</td>
<td>Pain from stimulus that would not normally produce pain</td>
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<tr>
<td>HYPERALGESIA</td>
<td>An increases response to a stimulus which is normally painful</td>
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<tr>
<td>DYSAESTHESIA</td>
<td>Unpleasant abnormal sensations, not necessarily painful</td>
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<tr>
<td>PARAESTHESIA</td>
<td>An abnormal sensation, but not unpleasant or painful</td>
</tr>
<tr>
<td>HYPERAESTHESIA</td>
<td>Increased sensitivity to stimulation</td>
</tr>
<tr>
<td>HYPERTHIA</td>
<td>Abnormal pain response to stimuli applied to an area of decreased sensitivity</td>
</tr>
<tr>
<td>HYPOAESTHESIA</td>
<td>decreased sensitivity to stimulation</td>
</tr>
<tr>
<td>HYPOALGESIA</td>
<td>decreased sensitivity to painful stimuli</td>
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<td>ANAESTHESIA</td>
<td>Lack of sensation</td>
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