Guideline for the Management of Neuropathic Pain in Primary Care

Introduction

Neuropathic pain is defined as "Pain caused by a lesion or disease of the somatosensory nervous system." The cause is very varied and may indeed be idiopathic. Neuropathic pain may often be suspected or identified through some of the classical descriptions of the pain that patients can give, such as: 'burning, shooting, tingling, electric shocks, sharp, nagging, walking on hot coals'. Common features are:

- Hyperalgesia – increased sensitivity to a normal pain stimulus, e.g. temperature
- Allodynia – pain created by a stimulus that does not ordinarily produce pain, e.g. application of a cotton swab, wearing of clothes
- Autonomic signs - skin changes such as oedema, shininess, change of perspiration
- Motor – dystonia, weakness and paralysis, and fasciculations.

Treatment is often difficult and tends to be aimed at management rather than cure. The mainstay of treatment is a multifactorial approach and as with any chronic condition patient education and participation is fundamental.

This guideline is for neuropathic pain only – it does not apply to other chronic pain conditions (e.g. general back pain).

If Complex Regional Pain Syndrome is suspected, refer early (see Appendix 1).

Pharmacological Interventions

Traditional analgesics may be of limited value in the management of neuropathic pain but that is not to say they should be avoided. The other point to note is that patients may get on better with one drug than another. It should also be recognised that the benefit of a treatment can be easily established by asking the patient whether they feel better on a specific treatment or not – unlike treating asymptomatic chronic conditions such as hypertension and diabetes.

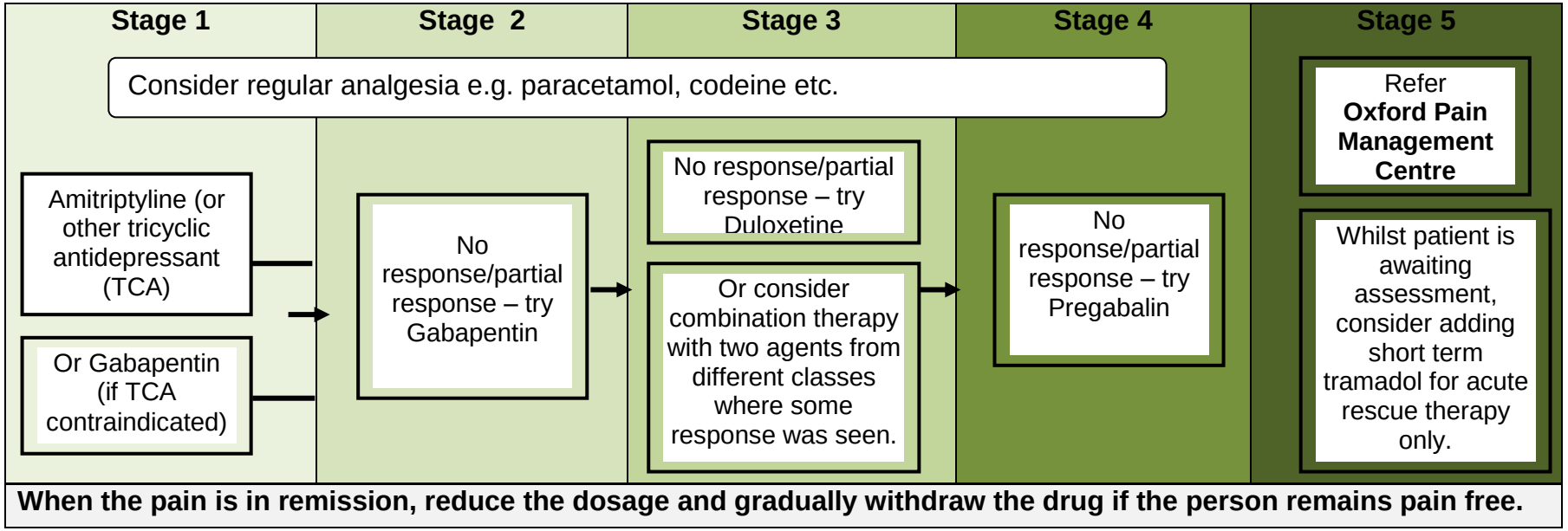
The Oxford Pain Management Centre

The Oxford Pain Management Centre at the Churchill Hospital is the current incarnation of one of the UK's original pain services. It is staffed by a group of consultants and a number of specialist nurses. It also has a clinical psychologist integrated within the team.

The Oxford Pain Management Centre offers a patient centred service that concentrates upon patient education and empowerment for the joint management of a chronic condition. It can advise on simple lifestyle changes and pharmacological management as well as interventional techniques where appropriate. Research is a constant aspect through its close links with the Pain Research Unit. The Oxford Pain Management Centre's fundamental role is to support colleagues in Primary Care, for referral information please visit : http://www.ouh.nhs.uk/services/referrals/pain/default.aspx

Treatment

It may be appropriate to initially try regular paracetamol or an NSAID. Simple analgesics are usually ineffective in pure neuropathic pain but may help with a coexisting nociceptive condition. Consider using the BPI questionnaire for a baseline assessment of symptoms (and for re-assessing) and agree an achievable pain relief goal with the patient (e.g. 30% pain relief or ability to undertake activities). **Trial each drug for at least 4-5 weeks at maximum tolerated dose**, before reviewing patient/diagnosis/treatment**.** For advice contact oxonpainadvice@nhs.net



All of the drugs in the guideline can cause significant adverse effects in some patients. If this occurs, try an alternative from the same therapeutic group

For referral criteria, exclusions and how to refer (including essential referral information) please visit: http://www.ouh.nhs.uk/services/referrals/pain/default.aspx. For advice contact oxonpainadvice@nhs.net

Drug choice and doses

Consider co-morbidities, side effects and potential for abuse before commencing treatments. Gabapentin and pregabalin have similar modes of action and adverse effects and should not be used together. Avoid using duloxetine and amitriptyline together.

Drug	Dosage	Titration and advice *(including approx. cost for 6 months, Drug Tariff March 2017)*
First Line		
Tricyclics		
Amitriptyline tablets	Initial dose: 10 to 25 mg Max Dose: 150 mg at night	• Increase by 10 to 25 mg weekly. Ensure patient tolerates dose at each step before increasing dose. • Advise patient to take at about 8pm; if morning sedation is problematic the dose may be taken earlier in the evening. • Pain relief may be seen after 7 days, however trial for at least 4-5 weeks if tolerated. • If it is not tolerated or is ineffective after the trial period, it should be withdrawn gradually over 1-2 weeks. *(50mg at night - £17)*
Imipramine tablets	Initial dose: 10 to 25mg Max dose: 75mg at night	Increase by 10 to 25 mg weekly. Ensure patient tolerates dose at each step before increasing dose. *(50mg at night - £12)*
Nortiptyline tablets	Initial dose: 10 to 25 mg Max dose: 75 mg at night	• Increase by 10 to 25 mg weekly. Ensure patient tolerates dose at each step before increasing dose. • May be better tolerated than amitriptyline *(50mg at night - £106)*
Second Line		
Anticonvulsants		
Gabapentin capsules	Initial dose: 300 mg Max dose: 1800 mg daily	• Increase by 300 mg every week to a max of 1800 mg daily. • In renal impairment, the elderly or drug sensitive patients, this titration may need to be done in 100mg increments. Refer to the SPC and bulletin 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 • **Use capsules** as tablets are considerably more expensive) • Gabapentin should not be stopped abruptly and should be reduced gradually over a minimum of one week, depending on dose and duration of treatment. *(300mg tds - £14)*
Other Considerations		
Duloxetine	Initial dose:	• Discontinue if inadequate response after trial

	60mg Max dose: 60mg	period, review treatment at least every 3 months. *(60mg od - £14)*
Pregabalin (Lyrica)	Initial dose: 75mg Max dose: 600mg daily	• Initially 150mg daily in 2 divided doses. Increase after 3- 7 days to 300mg & increase if necessary after 7 days to 600mg daily in 2 divided doses. • Always prescribe twice daily as this is more cost effective than three times a day dosing • **Must be prescribed by brand** when used for neuropathic pain **(LYRICA)** until directed otherwise. • It should not be stopped abruptly but should be reduced gradually over a minimum of one week. NB. All strengths of pregabalin cost the same. Prescribers should aim to minimise the capsule count by prescribing a twice daily regimen where possible. *(75mg bd - £386 , 300mg bd - £386)*
Tramadol capsules	Initial dose: 50 -100 mg Max dose: 400 mg daily	• 50 -100 mg 3 - 4 times daily • Consider tramadol only if acute rescue therapy is needed short term. Long-term use should be on advice from the specialist. *(100mg tds - £28)*
Alternative Options (may require advice of pain management centre)		
Topiramate	On specialist advice	
Lidocaine Patch	Apply up to three plasters	• Plaster should be worn for 12 hours, and then removed for 12 hours, in rotation. • Prescribe an initial 7 day trial, discontinue if no response. • Use in line with licensed indications post herpetic neuralgia only. *(Apply OD- £434)*
Capsaicin cream	Initial dose: 0.075% pea size amount four times/day for 6-8 weeks	Consider capsaicin cream for people with localised neuropathic pain who wish to avoid, or who cannot tolerate oral treatments. *(45g tube - £14.58)*
Morphine	Initial dose: 20 -120 mg Max dose: 120 mg daily	Initially 5 -20mg every 4 hours. Trial for 2 weeks, if no benefit is seen then stop as unlikely to improve by increasing dose. *See Opioids Aware Guidance.* *(Sevredol 10mg tds - £48)*

For trigeminal neuralgia only: Carbamazepine (first line)
This is one of several antiepileptics that can be of use for trigeminal neuralgia in addition to the tricyclic antidepressants and gabapentin etc.

- 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 and refer to Department of Neuroscience for further advice.

Common Side Effects:

- **Amitriptyline**- sedation, dry mouth, nausea, blurred vision. Seratonergic syndrome and cardiac side effects are both possible with TCAs especially in combination with SSRIs or tramadol medication. However, these are rare complications.
- **Duloxetine**- nausea, headache, dry mouth, sleepiness, dizziness
- **Gabapentin**- dizziness, somnolence, weight gain and oedema. Side effects are usually minor and subside within four weeks. Severe headaches do not tend to resolve, treatment should be reduced gradually.
- **Pregabalin** – drowsiness, dizziness, may cause confusion. Adverse reactions are usually mild to moderate in intensity
- **Tramadol**- nausea, constipation, dizziness, headache.
- **Topical treatments**- stinging, burning, redness, tenderness, swelling, rash.

Practical Prescribing and Management Points

- It is important to discuss with the patient at an early stage that complete elimination of neuropathic pain is often impossible. Reduction of pain to allow increased function would be a more realistic target. Trials of analgesics consider a 30-50% reduction in pain score a success. Patient expectation can be a lot higher than this.
- Tolerability and dose responses may be extremely variable amongst patients. If patients respond to lower-than-recommended doses, then there is no need to titrate up further.
- **Make only one change at a time in order to assess what medication is working (i.e. titrate down and stop the old medication before starting a new one).**
- **Stop drugs that aren't working and remove from repeat.**
- The natural history of painful neuropathy is only poorly understood and some patients may even see some spontaneous resolution of pain, enabling reduction of tablets and dosages.
- If the drug is effective, continue for 6 months and then consider dosage reduction and trial withdrawal to assess continuing benefit being obtained.
- Sign post to the Pain Toolkit for self-management advice
- Talking Space referral may be appropriate in patients with anxiety and depression.

For further information on Neuropathic Pain or Chronic Regional Pain Syndrome please do not hesitate to contact the Oxford Pain Management Centre
oxonpainadvice@nhs.net

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13. Pregabalin for acute and chronic pain in adults, Cochrane Database of Systematic Reviews, Moore 2009.
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17. NICE CG173 (Nov 2013) Neuropathic pain – pharmacological management: The pharmacological management of neuropathic pain in adults in non- specialist settings https://www.nice.org.uk/guidance/cg173
18. Presquipp – Neuropathic Pain Bulletins and template guidance on the management of neuropathic pain (Adults)

Appendix 1 – Complex Regional Pain Syndrome

If Complex Regional Pain Syndrome is suspected, refer early

The key symptom of CRPS is continuous, intense pain out of proportion to the severity of the injury (if an injury has occurred), which gets worse rather than better over time. CRPS most often affects one of the extremities (arms, legs, hands, or feet) and is also often accompanied by:

- "burning" pain
- increased skin sensitivity
- changes in skin temperature: warmer or cooler compared to the opposite extremity
- changes in skin color: often blotchy, purple, pale, or red
- changes in skin texture: shiny and thin, and sometimes excessively sweaty
- changes in nail and hair growth patterns
- swelling and stiffness in affected joints
- motor disability, with decreased ability to move the affected body part

Movement is the mainstay of management, but analgesia and education are necessary.

Appendix 2 – Licensed Drugs in Neuropathic Pain

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 is followed when treating neuropathic pain. This states:
"You should usually prescribe licensed medicines in accordance with the terms of their licence. However, you may prescribe unlicensed medicines where, on the basis of an assessment of the individual patient, you conclude, for medical reasons, that it is necessary to do so to meet the specific needs of the patient."
"When prescribing an unlicensed medicine you must:

a. be satisfied that there is sufficient evidence or experience of using the medicine to demonstrate its safety and efficacy,
b. take responsibility for prescribing the medicine and for overseeing the patient's care, monitoring, and any follow up treatment, or ensure that arrangements are made for another suitable doctor to do so,
c. make a clear, accurate and legible record of all medicines prescribed and, where you are not following common practice, your reasons for prescribing an unlicensed medicines

Drug	**Licensed Neuropathic Pain Indication** (as per SPC Feb 2017)
Amitriptyline tablets	Not licensed for any form of neuropathic pain
Imipramine tablets	Not licensed for any form of neuropathic pain
Nortiptyline tablets	Not licensed for any form of neuropathic pain
Gabapentin capsules	Gabapentin is indicated for the treatment of peripheral neuropathic pain such as painful diabetic neuropathy and post-herpetic neuralgia in adults.
Duloxetine	Indicated for the treatment of diabetic peripheral neuropathic pain.
Pregabalin (Lyrica)	Lyrica is indicated for the treatment of peripheral and central neuropathic pain in adults.
Tramadol capsules	Indicated for the treatment of moderate to severe pain.
Topiramate	Not licensed for any form of neuropathic pain
Lidocaine Patch	Versatis is indicated for the symptomatic relief of neuropathic pain associated with previous herpes zoster infection (post-herpetic neuralgia, PHN) in adults.
Capsaicin cream	Indicated for the symptomatic relief of neuralgia associated with and following Herpes Zoster infections (post-herpetic neuralgia) after open skin lesions have healed. Also, for the symptomatic management of painful diabetic peripheral polyneuropathy.
Morphine	Indicated for the relief of severe pain
Carbamazepine	Indicated for the paroxysmal pain of trigeminal neuralgia