



The Pharmacological Management of Neuropathic Pain in Adults

Susan McKernan

Midlands and Lancashire CSU

Approved December 2015

(Review date November 2018)

Version Control

Version Number	Amendments Made	Author	Date
Version 1.0	1 st version approved	SMcK	December 2015
Version 1.1	Lidocaine section: updated with unlicensed indications recommendation	SMcK	March 2016
Version 1.2	Neuropathic Pain PIL added, off label use of medicines PIL reformatted	AG/SMcK	June 16

Please Access via the LMMG Website to Ensure the Correct Version is in Use.

Contents

1.INTRODUCTION	2
2.PURPOSE AND SUMMARY	2
3.SCOPE	3
4. GUIDANCE	3
4.1 'Off License' use of Medications.....	3
4.2 Initial Patient Assessment	3
4.3 Neuropathic Pain Treatment Algorithm	4
4.4 Prescribing Information	5
5.REFERENCES	9
APPENDIX 1: Patient information –Use of medicines outside their Marketing Authorisation	11
APPENDIX 2: Patient information - Neuropathic Pain... ..	12

1. INTRODUCTION

Neuropathic pain can arise from damage to the nerve pathways at any point and can be classified as central (originating from damage to the brain or spinal cord) or peripheral (originating from the peripheral nervous system)¹.

It is often unresponsive to conventional analgesics. Treatment centres around the use of adjuvants that affect the nervous system, namely antidepressant and antiepileptic medications. Many of these commonly used treatments are not licensed for neuropathic pain and historically there has been considerable variation in how treatment is initiated, the doses used and the order which medications are introduced¹.

Some patients have difficulty communicating and may be reliant on third parties to detect that they are in pain. This will require the use of non-verbal pain rating scales. In the cognitively impaired, inadequately treated pain can lead to behavioural problems, anxiety and depression. Therefore before prescribing medications to manage behaviour, it is important that clinicians and carers consider the possibility that a person may be experiencing pain.² See Appendix 1 for more information and examples of pain assessment tools.

It should be emphasised that medicines play only one part in managing pain. Maintaining fitness, pacing activities and a generally healthy lifestyle are also important.^{1,3}

2.PURPOSE AND SUMMARY

To provide guidance on the pharmacological management of neuropathic pain in adults.

3.SCOPE

This guideline provides recommendations on the medical management of adults with neuropathic pain. The outlined treatment strategy is relevant to both specialist and non-specialist settings.

It does not cover:

- Management of pain which is not neuropathic. (See LMMG [chronic non-cancer pain guidance](#))
- The management of pain in palliative care.
- Specialist medicines or medication regimens, which will continue to be supplied from secondary care.
- Prescribing of analgesics within secure prison services. See the Royal College of GP: [Safer Prescribing in Prisons](#).¹¹

4. GUIDANCE

Prescribers should use this guidance in conjunction with the medication's summary of product characteristics ([SPC](#)) and the British National Formulary ([BNF](#)).

4.1 'Off License' use of Medications

This guideline recommends use of some licensed medications for unlicensed indications. In this instance, prescribers should follow relevant guidance around this taking responsibility for the decision and being satisfied that use best serves the patients individual needs. The patient should provide informed consent, which should be documented.^{1,4,21-22}

For more information see the British Pain Society's '[Use of medicines outside of their UK marketing authorisation in pain management and palliative medicine](#)' General Medical Council's '[Good practice in prescribing and managing medicines and devices](#)'²¹ and [Appendix 1](#) for patient information.²²

Amitriptyline	Not currently licensed for neuropathic pain, but use is supported by NICE CG173
Gabapentin	Licensed for peripheral neuropathic pain e.g. Painful diabetic neuropathy and post-herpetic neuralgia in adults.
Pregabalin (Lyrica ® brand only)	Licensed for peripheral and central neuropathic pain.
Duloxetine	Licensed for diabetic peripheral neuropathic pain.
Capsaicin cream 0.075%.	Licensed for post-herpetic neuralgia after open skin lesions have healed and painful diabetic peripheral polyneuropathy
Capsaicin cream 0.025%	Licensed as an adjunct in hand or knee osteoarthritis. Not licensed for neuropathic pain
Carbamazapine	Licensed for trigeminal neuralgia only
Lidocaine 5% plaster	Licensed for post herpetic neuralgia

4.2 Initial Patient Assessment^{1&3}

Ensure accurate diagnosis of neuropathic pain and appropriate management of underlying condition. If required use validated [tools](#) or [questionnaires](#).⁶⁻⁷

Consider:

- The aetiology and severity of pain
- Analgesic history
- Impact on lifestyle & daily activities/ participation
- Common psycho-social problems. The patients' perceptions of the pain and its cause; coping strategies, mood changes, quality of sleep, and anxiety can all impact on perceived pain. Addressing these might reduce the need for analgesics³.

All Neuropathic Pain (Excluding Trigeminal Neuralgia)

Step 1: Amitriptyline

(Patient information is available [here](#))⁸

Start at 10mg at night, increase by 10mg every 3-7 days according to effect & tolerability

Usual Therapeutic Dose Range: 25-75mg at night ^{5&10}
There is limited evidence of effectiveness of doses >75mg (use only on the advice of pain services)

Duration of adequate trial: 6-8 weeks with at least 2 weeks at the maximum tolerated dose¹⁰

Do not stop abruptly Reduce gradually over 4 weeks (or 6 months if taking long term)⁵

Contraindicated in arrhythmias, severe liver disease, recent MI & manic phase of bipolar disorder.⁵

Can be used in combination with gabapentin or pregabalin if there is a partial response to either or both medications.*



Step 2: Gabapentin

See also [SPC and Section 4.4](#)

Start at 300mg at night, titrate upwards until efficacy achieved or not tolerated. Reduced doses required in [renal impairment](#).

The rate of increase should be guided by patient & tolerability.

Usual Therapeutic Dose Range: 300mg-3600mg daily in three divided doses

Duration of adequate trial: 3-8 weeks for titration plus 2 weeks at maximum tolerated dose.

Do not stop abruptly. Decrease gradually over 1-2 weeks



Step 3: Pregabalin (Lyrica ®)

See also [SPC and Section 4.5](#)

Start at 75mg twice daily, titrate upwards until efficacy achieved or not tolerated. Reduced doses required in [renal impairment](#).

The rate of increase should be guided by patient & tolerability.

Usual Therapeutic Dose Range: 150-600mg daily in divided doses

Duration of adequate trial: 3-8 weeks for titration plus 2 weeks at maximum tolerated dose.

Do not stop abruptly. Decrease gradually over 1-2 weeks

Or Consider Duloxetine (If diabetic neuropathy)

Avoid if CrCl <30ml/minute

See [MHRA safety warning for Duloxetine](#); re: cases of suicidal ideation

Start at 60mg daily (a 30mg starting dose may be appropriate for some patients). Increase to 60mg twice daily after 1 week if needed.

Duration of adequate trial: 8 weeks with at least 4 weeks at maximum tolerated dose.

Do not stop abruptly. Decrease dose gradually over 1-2 weeks

If the first choice is not tolerated or ineffective, discontinue and try the other drug

Treatment of Trigeminal Neuralgia

Use Carbamazepine 1st line^{1&9}

Start at 100mg twice daily (prescribe generically)

Titrate slowly e.g. by 100mg every 3 days to 1600mg in divided doses. (MR preparations may be useful at night if the person experiences breakthrough pain).

If there is inadequate response or treatment is not tolerated **consider early referral to a specialist pain or condition specific service**¹

Post- Herpetic Neuralgia

(Associated with previous herpes zoster infection)

Treat initially with standard oral therapies as per steps 1-3 and topical capsaicin (unless contraindicated or not tolerated).

If standard therapies fail, or lead to intolerable side effects, consider lidocaine 5% medicated plasters, these are approved for primary care initiation when used to treat post-herpetic neuralgia. **See section 4.4.4 for prescribing information**

TOPICAL TREATMENTS

Consider **capsaicin cream** for patients with **localised neuropathic pain** who wish to avoid, or who cannot tolerate oral treatments.¹

To minimise side-effects start at 0.025% pea size amount four times daily for 6-8 weeks & increase if tolerated to 0.075% four times daily.

Duration of adequate trial: Pain relief begins within the 1st week and increases with continuing use, over the next 2-8 weeks¹

Reviewing Treatment

Titrate medications to the maximum tolerated dose.

If there is no useful response after an adequate trial or the medication is not tolerated reduce and stop before replacing/moving to the next step. Tapering will minimise the risk of discontinuation symptoms.^{1&10}

Monitor LFTs, FBC, Renal function & depression

When **introducing a new treatment**, take into account any overlap with the old treatments to avoid deterioration in pain control.^{1&10}

Consider the possibility of a mixed pain presentation. Refer to the [chronic non-cancer pain guidelines](#) for more information on the management of nociceptive pain

See section 4.4.5-4.4.6 for information regarding use of tramadol and nortriptyline in neuropathic pain.

* NICE CG 173 does not make a recommendation re: use of combination treatments because there is a lack of evidence of effectiveness, however the NICE clinical development group noted it may be more practical and more effective than switching treatment and may reduce adverse effects of the individual drugs.^{1&10}

4.4 Prescribing Information

4.4.1 Gabapentin^{1,5,10,13}

Dose titration. Various titrations may be used, depending on the person taking it and how well they tolerate it.¹⁰ Suggested regimens are detailed below.

Table 1. Gabapentin titration regimen

Usually suitable for older or frail adults

	Day 1	Day 2	Day 3	Day 4	Day 5	Day 6	Day 7
Morning				100mg	100mg	100mg	100mg
Midday							100mg
Night	100mg						
Morning	Day 8 100mg	Day 9 100mg	Day 10 100mg	Day 11 100mg	Day 12 100mg	Day 13 100mg	Day 14 200mg
Midday	100mg	100mg	100mg	100mg	100mg	100mg	200mg
Night	100mg	100mg	100mg	100mg	100mg	100mg	200mg
Morning	Day 15 200mg	Day 16 200mg	Day 17 200mg	Day 18 200mg	Day 19 200mg	Day 20 200mg	Day 21 200mg
Midday	200mg						
Night	200mg						

Day 22 onwards: Dose may be increased by 300mg/day, ideally at weekly intervals as tolerated up to a maximum of 3600mg

(For patients with renal impairment, See dose recommendations above).

Dose increases are only required if the patient has not achieved adequate pain relief.

Prior to increasing doses some pain relief or improvement in functioning should be demonstrated otherwise it may lead to inappropriate use of escalated doses which are not effective

Where possible the patient should have ownership of the titration process and be given sufficient information and support to do this.

Patients should be advised of side effects including drowsiness which may affect their ability to drive and how these can be managed or reduced. E.g. By taking the largest dose at night and by slowing the titration process if needed.

Patient information is available [here](#)¹⁴

Table 2. Gabapentin titration regimen

Usually suitable for otherwise healthy, younger adults¹⁰

	Day 1	Day 2	Day 3	Day 4	Day 5	Day 6	Day 7
Morning		300mg	300mg	300mg	300mg	300mg	300mg
Midday			300mg	300mg	300mg	300mg	600mg
Night	300mg	300mg	300mg	300mg	600mg	600mg	600mg
Morning	Day 8 300mg	Day 9 600mg	Day 10 600mg	Day 11 onwards Dose may be increased by 300mg/day, at 3 day intervals up to a maximum of 3600mg (For patients with renal impairment, See dose recommendations above).			
Midday	600mg	600mg	600mg				
Night	600mg	600mg	600mg				

The BNF suggests an accelerated titration regimen i.e. starting at 300mg three times per day and increasing by 300mg every 2-3 days according to response. In practice this regimen is limited by side effects, therefore it should be reserved for use in a restricted patient group, of particularly fit, healthy adults who have a clear understanding of the titration process and potential side effects, including drowsiness which may affect their ability to drive.

General Prescribing Points

- Can cause weight gain, which should be taken into consideration when selecting therapy for certain people e.g. patients with diabetes¹⁰
- There are increasing reports around the **abuse potential** of both gabapentin & pregabalin. Advice for prescribers on the risk of misuse is available [here](#) from Public Health England^{11,12}
- An **adequate trial requires 3-8 weeks for titration** plus 2 weeks at maximum tolerated dose¹⁰
- **Do not stop abruptly.** Decrease gradually over 1-2 weeks
- **Can be used in combination with amitriptyline** (if there has been a partial response to either or both treatments)*

Dose reduction required in renal impairment

eGFR (ml/min) ⁵	CrCl (ml/min) ¹³	Total daily dose (mg/day) (Taken in three divided doses)
-	≥ 60	900-3600mg
50-80	50-59	600-1800mg
30-50	30-49	300-900mg
15-30	15-29	150 (given as 300mg alternate days) -600mg
<15	<15	Reduce daily dose in proportion to CrCl.

* NICE CG 173 does not make a recommendation re: use of combination treatments because there is a lack of evidence of effectiveness, however the NICE clinical development group noted it may be more practical and more effective than switching treatment and may reduce adverse effects of the individual drugs.^{1 & 10}

4.4.2 Pregabalin (Lyrica®) ^{1,5,10,&14}

Pregabalin dose titration.

Various titrations may be used, depending on the person taking it and how well they tolerate it. A Suggested regimen is detailed

Table 3. Pregabalin Titration Regimen

Start at day 1 for older or frail adults, for otherwise healthy younger adults start at day 15.

	Day 1	Day 2	Day 3	Day 4	Day 5	Day 6	Day 7
Morning	25mg						
Night	25mg						
	Day 8	Day 9	Day 10	Day 11	Day 12	Day 13	Day 14
Morning	50mg						
Night	50mg						
	Day 15	Day 16	Day 17	Day 18	Day 19	Day 20	Day 21
Morning	75mg						
Night	75mg						
	Day 22	Day 23	Day 24	Day 25	Day 26	Day 27	Day 28
Morning	150mg						
Night	150mg						
Day 29 onwards: 300mg twice daily							

PREGABALIN capsules cost the same amount regardless of which strength capsule is used. Using **TWICE DAILY administration** improves the **COST EFFECTIVENESS** of treatment.

Dose increases are only required if the patient has not achieved adequate pain relief.

Prior to increasing doses some pain relief or improvement in functioning should be demonstrated otherwise it may lead to inappropriate use of escalated doses which are not effective.

Where possible the patient should have ownership of the titration process and be given sufficient information and support to do this.

They should be advised of side effects including drowsiness which may affect their ability to drive and how these can be managed or reduced. E.g. By taking the largest dose at night and by slowing the titration process if needed.

Patient information is available [here](#) ¹⁶

General Prescribing Points

- Can cause weight gain, which should be taken into consideration when selecting therapy for certain people for example patients with diabetes¹⁰
- There are increasing concerns around the **abuse potential** of **GABAPENTIN** and **PREGABALIN**. It has been noted that it seems easier to achieve a recreational high with pregabalin than gabapentin: Advice for prescribers on the risk of misuse is available [here](#) from Public Health England^{11,12}
- An **adequate trial requires 3-8 weeks for titration** plus 2 weeks at maximum tolerated dose
- **Do not stop abruptly.** Decrease gradually over 1-2 weeks
- Can be used in **combination with amitriptyline** (if there has been a partial response to either or both treatments)
- Can cause QT prolongation¹⁵
Nb. NICE CG 173 does not make a recommendation re: use of combination treatments because there is a lack of evidence of effectiveness, however the NICE clinical development group noted it may be more practical and more effective than switching treatment and may reduce adverse effects of the individual drugs ^{1 & 10}

Pregabalin Dose Recommendation in Renal Impairment

eGFR (ml/min) ⁵	CrCl (ml/min) ¹⁵	Starting dose (mg/day)	Maximum Dose (mg/day)
≥60	≥60	150mg (In 2 divided doses)	600mg (In 2 divided doses)
≥30-≤ 60	≥30-≤ 60	75mg (In 2 divided doses)	300mg (In 2 divided doses)
≥15-≤ 30	≥15-≤ 30	25-50mg (Once daily or in 2 divided doses)	150mg (Once daily or in 2 divided doses)
<15	<15	25mg (Once daily)	75mg (Once daily)

4.4.3 Switching between Gabapentin and Pregabalin¹⁷⁻¹⁹

Gabapentin and pregabalin are structurally similar and act on the voltage-gated calcium channels in the central nervous system.¹⁷

There is conflicting opinion regarding the appropriateness of directly switching between the two treatments:

- The manufacturer of both pregabalin and gabapentin advise that if they are to be discontinued, or substituted with an alternative medication, the dose should be tapered gradually over a minimum of a week.¹³⁻¹⁵ This is to minimize risk of seizures when they are being used as anticonvulsants.¹⁸
- NICE recommend that when withdrawing or switching between neuropathic pain treatments that the withdrawal regimen is tapered to take account of dosage and any discontinuation symptoms.¹
- There is trial data that shows that a direct switch between gabapentin and pregabalin is possible when treating neuropathic pain.¹⁷ More information is available from [UKMI Q&A 408.2](#).¹⁸

Points to Consider if Switching

- Direct switches are outside the terms of the product license but there are studies which support this strategy.¹⁸
- Dose equivalence tables have been constructed assuming pregabalin to have six times the pharmacological effect of gabapentin. **This is a crude approximation due to the non-linear pharmacokinetics of gabapentin.**¹⁶

Approximate Pregabalin: Gabapentin Equivalencies ¹⁶	
Pregabalin total daily dose (given in 2 divided doses)	Gabapentin total daily dose (given in 3 divided doses)
150mg	900mg
225mg	901-1500mg
300mg	1501-2100mg
450mg	2101-2700mg
600mg	2701-3600mg
Please see notes below about switching from gabapentin to pregabalin	

- Pregabalin has linear kinetics and an increase in dose results in a proportional increase in drug absorption and pharmacological effect. This means that a direct switch to gabapentin can be made, but a dose reduction should be considered if the patient has been experiencing side effects.¹⁷ Direct switching from pregabalin to gabapentin has been employed successfully by many local organisations as part of a cost saving exercise.
- **A direct conversion from gabapentin to pregabalin may not always be appropriate because of its non-linear pharmacokinetics** (the fraction of gabapentin absorbed decreases as the dose is increased). This means that there will not always be a linear correlation between dose equivalents.¹⁷ It is therefore recommended that extra care is taken if switching from gabapentin to pregabalin and that treatment is tapered as per NICE recommendations.
- Studies which support a direct switch have discontinued one therapy after an evening dose and initiated the alternative therapy the following morning.¹⁶

4.4.4 Lidocaine 5% Plaster (Versatis®) ¹⁹

All patients with neuropathic pain (regardless of cause) should initially be managed as per the treatment algorithm outlined in section 4.2.

- **For patients with post-herpetic neuralgia** (associated with previous herpes zoster infection). If standard neuropathic treatments as per section 4.2 do not provide sufficient analgesia or have led to intolerable side-effects, lidocaine patches may be initiated in primary care. (i.e. Green colour classification).
- **For patients with localised neuropathic pain with a predominance of allodynia and/or hyperalgesia and dysesthesias** (not associated with previous herpes zoster infection). If standard neuropathic agents as per section 4.2 do not provide sufficient analgesia or have led to intolerable side-effects, lidocaine patches may be prescribed within specialist services only. Primary care initiation or continuation of treatment is not recommended (i.e. Red colour classification). **N.b. Please check local formularies before prescribing.**

It is recognised that there may be an historic cohort of patients who have been prescribed lidocaine plasters from primary care services. These patients should have the opportunity to continue treatment until it is deemed clinically appropriate to stop.

Prescribing information. Lidocaine 5% Plaster (Versatis®)

Dose: The painful area should be covered with the plaster once daily for up to 12 hours within a 24 hours period. Only the number of plasters that are needed for an effective treatment should be used. When needed, the plasters may be cut into smaller sizes with scissors prior to removal of the release liner. **In total, not more than three plasters should be used at the same time.**

Treatment outcome should be re-evaluated after 2-4 weeks

Long-term clinical studies showed that the number of plasters used decreased over time. Therefore treatment should be reassessed at regular intervals to decide whether the amount of plasters needed to cover the painful area can be reduced, or if the plaster-free period can be extended.

Instructions for use: Each plaster must be worn no longer than 12 hours. The subsequent plaster-free interval must be at least 12 hours.

The plaster must be applied to the skin immediately after removal from the sachet and following removal of the release liner from the gel surface. Hairs in the affected area must be cut off with a pair of scissors (not shaved).

4.4.5 Tramadol

NICE recommend that tramadol is only prescribed as acute rescue analgesia by non-specialists (whilst awaiting referral to pain services) or it is used longer term on the advice of a specialist. This is because trial data is only available up to 4 weeks, evidence of long-term benefit is lacking and there are high rates of withdrawal due to adverse effects. ^{1&10}

Prescribers should also be aware of its potential for interaction with other medications e.g. when used in combination with amitriptyline or duloxetine, there is a low risk of **serotonin syndrome** (features include confusion, delirium, shivering, sweating, changes in BP and myoclonus). ⁵

All tramadol prescriptions need to comply with controlled drug prescription writing requirements. ¹⁰

4.4.6 Nortriptyline

The NICE neuropathic pain, guideline development group, found estimates of nortriptyline's effectiveness to be highly uncertain, because of this they were not able to make a recommendation regarding its use. In the absence of a consistent evidence base, it has not been included in the LMMG neuropathic pain guidance and it is expected that patients will be treated as per section 4.2.

4.4.7 Sativex®

Sativex® is an oromucosal cannabinoid spray which is licensed for spasticity symptom improvement in Multiple Sclerosis (MS).²⁰ There is increasing interest in its potential for use in chronic refractory pain of other neurological origin. Until such time as a local review of the evidence has been completed which defines a place in therapy, it is expected that prescribing for new patients will be in the context of a clinical trial and prescribing for existing patients will remain the responsibility of the secondary care organisation.

5. REFERENCES

1. NICE CG 173 *neuropathic pain- pharmacological management*. (Full guidance). November 2013. <https://www.nice.org.uk/guidance/cg173/evidence/neuropathic-pain-pharmacological-management-full-guideline-191621341>
2. Royal College of Physicians, British Geriatrics Society and British Pain Society. *The assessment of pain in older people: national guidelines*. Concise guidance to good practice series, No 8. London: RCP, 2007.
3. SIGN 136. *Management of Chronic Pain*. December 2013. <http://www.sign.ac.uk/pdf/SIGN136.pdf>
4. GMC. *Prescribing Guidance: Prescribing Unlicensed Medicines*. Good medical practice 2013. http://www.gmc-uk.org/guidance/ethical_guidance/14327.asp
5. British National Formulary (online) London: BMJ Group and Pharmaceutical Press Accessed March 2015
6. Bennet et al. *The S-LANSS score for identifying pain of predominantly neuropathic origin: Validation for use in clinical and postal research*. The Journal of Pain. Vol 6 149-158 2005. <http://www.specialistpainphysio.com/wp-content/uploads/2010/07/S-LANNS.pdf>
7. Freynhagen et al. *Pain Detect. Pain Questionnaire*. Curr Med Res Opin, Vol 22. No. 10. <http://www.specialistpainphysio.com/wp-content/uploads/2010/07/painDETECT-Questionnaire-01.pdf>
8. The British Pain Society. *Information for adult patients prescribed amitriptyline for the treatment of pain*. Version 1. June 2014 https://www.britishpainsociety.org/static/uploads/resources/files/FPM_Amitriptyline.pdf
9. Pan Mersey Area prescribing committee. *Neuropathic pain guidelines. Pharmacological management in non-specialist settings*. Version 1. <http://www.panmerseyapc.nhs.uk/guidelines/documents/G1378.pdf>
10. Clinical Knowledge Summaries. *Neuropathic Pain-drug treatment*. Last revised June 2015. Accessed March 2015 via <http://cks.nice.org.uk/neuropathic-pain-drug-treatment#!scenario>
11. RCGP *Safer Prescribing in Prisons: Guidance for clinicians-* RCGP secure environments group. November 2011
12. Public Health England. *Advice for prescribers on the risk of the misuse of pregabalin and gabapentin*. NHS England. https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/385791/PHE-NHS_England_pregabalin_and_gabapentin_advice_Dec_2014.pdf
13. The Electronic Medicines Compendium. *Gabapentin 100mg capsules*. Last updated 23/07/14. Accessed March 2015 <https://www.medicines.org.uk/emc/medicine/25430>
14. The British Pain Society. *Information for Adult Patients Prescribed Gabapentin for the treatment of Pain*. Version 1. June 2014 https://www.britishpainsociety.org/static/uploads/resources/files/FPM-Gabapentin_0.pdf
15. The Electronic Medicines Compendium. *Lyrica Capsules*. Last updated 27/04/15. Accessed May 2015. <https://www.medicines.org.uk/emc/medicine/14651>
16. The British Pain Society. *Information for Adult Patients Prescribed Pregabalin for the Treatment of Pain*. Version 1. June 2014 https://www.britishpainsociety.org/static/uploads/resources/files/FPM-Pregablin_2.pdf
17. The Australian Pain Society *Conversion of Gabapentin: Simple and Easy!* Newsletter, Vol 33 Issue 5. https://www.apsoc.org.au/PDF/Newsletters/APS_Newsletter_JUL13.pdf
18. UKMI Q&A 408.1 *How do you switch between pregabalin & gabapentin for neuropathic pain and vice versa?* 2012 <http://www.evidence.nhs.uk/search?q=%22How+do+you+switch+between+pregabalin+and+gabapentin+for+neuropathic+pain%2C+and+vice+versa%22>
19. The Electronic Medicines compendium *Versatis 5% Medicated Plaster* last updated 27/04/2015 accessed March 2015 <https://www.medicines.org.uk/emc/medicine/19291>

20. Medicines compendium Sativex Oromucosal Spray last updated 20/05/2015 accessed <https://www.medicines.org.uk/emc/medicine/23262>
21. General Medical Council. Prescribing Guidance: Prescribing unlicensed medicines. 2013. Accessed Via: http://www.gmc-uk.org/guidance/ethical_guidance/14327.asp
22. The British Pain Society: Use of medicines outside of their UK marketing authorisation in pain management and palliative medicine. September 2013. Accessed via: https://www.britishpainsociety.org/static/uploads/resources/files/useofmeds_professional_final.pdf

© Midlands and Lancashire Commissioning Support Unit, 2016. The information contained herein may be superseded in due course. All rights reserved.

Produced for use by the NHS, no reproduction by or for commercial organisations, or for commercial purposes, is allowed without express written permission.

Midlands and Lancashire Commissioning Support Unit,
Jubilee House, Lancashire Business Park, Leyland, PR26 6TR

Tel: 01772 214 400 | www.midlandsandlancashirecsu.nhs.uk

This guidance does not override the individual responsibility of health professionals to make decisions in exercising their clinical judgement in the circumstances of the individual patient, in consultation with the patient and/or guardian or carer. For full prescribing information please refer to the BNF and SPC ensuring correct SPC according to dose is consulted.

Use of medicines outside of their UK Marketing Authorisation in pain management



This leaflet explains how some medicines are used differently to how they were originally developed and approved

How are medicines approved for use in the United Kingdom?

In the UK, medicines must have a licence, also called a Marketing Authorisation (MA), before they are approved for treating patients. The licence is confirmation that the medicine has been tested for safety and is of an appropriate quality. It also outlines what conditions the medicine is approved for use in, what the doses should be and any precautions for its use.

What do the terms 'off-Label' and 'off-License' mean?

The licence does not prevent a doctor from prescribing the medicine for other uses as long as the doctor is satisfied that it is effective and safe in those circumstances. This is known as 'off-label' or 'off-license' use.

Why are medicines used 'off-label' or 'off-license'?

Sometimes evidence shows that a medicine can also be used in circumstances outside of its original licence; and there may be clinical situations, when the 'off-label' use of medicines, may be judged to provide you with the most suitable treatment.

For example, the antidepressant amitriptyline is effective at treating certain types of pain, but it does not have a license for this use.

What differences might I notice if I am prescribed or supplied with an off-label medicine?

In certain settings, because off-label or unlicensed medicines are so often used, it may not be highlighted to you. However, at other times, your doctor or pharmacist will point out that you are being given an off-label or unlicensed medicine, explain why it is the preferred treatment and discuss its safety and effectiveness with you.

If you are given any further written information, please read it carefully.

You may notice that a manufacturer's information leaflet supplied with the medicine is not specific to you. For example, you may notice that it does not include information about the condition for which you are being treated, or it may state a dose that is different from that which the doctor has prescribed.

A common example of this is the use of certain antidepressant and epilepsy medicines to treat pain. These have a licence for the treatment of depression or epilepsy but not pain and so the information leaflet enclosed with the medicine does not refer to pain.

What should I do if I have any concerns about the medicine I have been given?

Whether within licence or not, whoever prescribes you the medicine should also provide you with a clear explanation of how to take it, the expected benefits and possible side effects.

If you experience a side effect from any medicine, you should first tell your doctor or another member of the health-care team.

You are also encouraged to report any side effects using the Yellow Card Scheme – go to www.mhra.gov.uk to find out more.

What do I do if I want more information?

Please talk to your doctor or pharmacist. They are knowledgeable and experienced with medicines and will be pleased to answer your questions.

For More Information Contact:

Name:

Telephone:

Job Role:

Version 1.1

Midlands and Lancashire CSU

Approved: September 2015

Review date: September 2018

Patient Information Leaflet – Neuropathic Pain

What is neuropathic pain?

Neuropathic pain or 'nerve pain' is pain that occurs because of damage or changes to nerves.

Damage to nerves can occur for many different reasons and your doctor may wish to discuss this with you in more detail.

Neuropathic pain can also develop as a result of changes to nerves that develop over time. Nerves are continually changing based on our experiences and learning and sometimes these changes can result in the development of pain or abnormal sensations. This process is called 'neuroplasticity'.

The nerves effected could potentially be anywhere in the body. However, nerve pain in the legs and feet is more common. [1]

What are the symptoms of neuropathic pain?

Common symptoms of neuropathic pain include:

- Pins and needles;
- A burning or sharp pain usually in the feet and legs;
- Feeling pain from something that should not be painful at all, i.e. very light touching. [1]

How long will I have neuropathic pain for?

This can vary considerably and depends upon the cause of the nerve damage. Some cases of neuropathic pain may

References

[1] NHS, "Peripheral Neuropathy - Symptoms," NHS, 02 July 2014. [Online]. Available: <http://www.nhs.uk/Conditions/Peripheral-neuropathy/Pages/Symptoms.aspx>. [Accessed 11 April 2016].

improve with time if the underlying cause is treated. However, in some cases, neuropathic pain is permanent and can even become progressively worse over time. [1]

Your doctor will be able to provide you with further advice.

What treatments are available for neuropathic pain?

Abnormal sensations due to nerve damage may not require medication. Nerve pain may respond to typical pain killers, for example paracetamol or ibuprofen. However, medicines that act on the nerves themselves may be needed. There are many different types of nerve medicines available and your doctor will discuss treatment options, including the risks and benefits of each, with you before you start to take your medicine.

What are the alternatives to taking oral medicines?

As discussed, there are medicines that can be taken to treat neuropathic pain but there are also alternative treatments to oral medicines that can be useful:

Topical medicines can be used if your neuropathic pain is localised to a particular area of the body.

Other pain management techniques can help to reduce the distress associated with abnormal neuropathic sensations. This may include alternative therapies to medicines such as: psychological therapies, postural training and increased fitness and exercise. These treatments can often be a better method of management of the pain than taking medication.

Your doctor will be able to advise you if any alternative treatments might be suitable for the management of your pain.

What happens if I am still in pain?

If your doctor has started a medicine for your nerve pain and **after 6 – 8 weeks** you are still in pain your doctor will discuss alternative treatments with you. These may include prescribing you another medicine and carefully stopping the first medicine, or discussing alternative pain management strategies.

What about side effects?

Unfortunately, all medicines have the potential to cause side effects. Sometimes the medicines that are used to treat nerve pain can have side effects associated with them.

Your doctor will be aiming to treat your pain with the medicine that causes the least number of side effects. It is important that if you experience any side effects and you are thinking about stopping your medication to discuss this with your doctor or pharmacist first.

Some medicines cannot be stopped suddenly and your doctor or pharmacist can advise you regarding stopping medication safely.

Once discontinued, your doctor has the option of prescribing another medicine to control your pain

If you are given any further written information, please read it carefully.

You may notice that a manufacturer's information leaflet supplied with the medicine is not specific to you. For example, you may notice that it does not include information about the condition for which you are being treated, or it may state a dose that is different from that which the doctor has prescribed.

A common example of this is the use of certain antidepressant and epilepsy medicines to treat pain. These have a licence for the treatment of depression or epilepsy but not pain and so the information leaflet enclosed with the medicine does not refer to pain.

If you are unsure what you are taking your medicine for, please discuss this with your pharmacist or doctor.

You are also encouraged to report any side effects using the Yellow Card Scheme – go to www.mhra.gov.uk to find out more.

What do I do if I want more information?

Please talk to your doctor or pharmacist. They are knowledgeable and experienced with medicines and will be pleased to answer your questions.

For More Information Contact:

Name:

Telephone:

Job Role:

Version 1.0

Midlands and Lancashire CSU

Approved 9th June 2016

References

[1] NHS, "Peripheral Neuropathy - Symptoms," NHS, 02 July 2014. [Online]. Available: <http://www.nhs.uk/Conditions/Peripheral-neuropathy/Pages/Symptoms.aspx>. [Accessed 11 April 2016].