Guidelines for the Prescribing of:
The Initiation, Management and Discontinuation of Pregabalin and Gabapentin prescribing for neuropathic pain in Primary Care

1. BACKGROUND

Neuropathic pain (NeP) is defined as a pain arising as a direct consequence of a lesion or disease affecting the somatosensory system. While nociceptive pain is produced by direct damage to the tissues involved, abnormally stimulated nerves are believed to play a key role in NeP.
This can result from nerve damage caused by trauma or certain conditions: Diabetes - Herpes zoster (shingles) - Trigeminal neuralgia.
NeP 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'. The pain is often worse at night, and may be paroxysmal or continuous. Characteristic signs and symptoms 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 include skin changes such as oedema, shininess, change of perspiration Motor – dystonia, weakness and paralysis, and fasciculations.
Patients beliefs and perceptions of the pain and its cause, coping strategies, mood changes, disturbed sleep, and anxiety all need to be addressed. Therefore, treating anxiety or depression first might also reduce the need for analgesics.

Pregabalin and gabapentin have a well-defined role in the treatment neuropathic pain as per NICE CG173 and local prescribing guidelines. Prescribers should also be aware that use of pregabalin and gabapentin can lead to dependence and may be misused or diverted as highlighted in recent Public Health England Advice.
https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/385791/PHE-NHS_England_pregabalin_and_gabapentin_advice_Dec_2014.pdf

From 1st April 2019, gabapentin and pregabalin will be reclassified as Schedule 3 controlled drugs under the Misuse of Drugs Regulations 2001.

2. Aim

The principal aim of these guidelines is to provide additional information to enable non specialist GP prescribers to initiate and manage treatment of patients with gabapentin and pregabalin prior to patients' referral to specialist clinics in line with the local HERPC guidelines managing chronic non-malignant pain in adults.

3. Initiation

These guidelines for management of chronic non-malignat pain, including NeP can be found at **http://www.hey.nhs.uk/herpc/guidelines/analgesiaalgorithm.pdf**

The guidelines for neuropathic pain (not diabetic neuropathy) recommend gabapentin as 1st or 2nd line treatment. Pregabalin is recommended only if gabapentin is not tolerated.

Prescribers should set realistic expectations and treatment goals. Achieving pain free status is not always achievable. Reduction in pain by 50% is a commonly used endpoint in clinical trials. Screening tools can also be useful to aid diagnosis: the Neuropathic Pain Scale (Appendix 1) 1 to 10 is a well-known validated scale. Evidence supports the validity of the scale items for detecting change in pain after treatments.

It is useful to have an indication of when to stop a medication. There is a period of dose titration to response. If there has been no response to treatment within two-to four weeks, after titration to adequate dose, patients are unlikely to develop a response thereafter. Integral to success is regular re-assessment of the patient and stopping medication that is not working effectively.
Nice Guidelines:Neuropathic pain-pharmacological management -NICE guidelines CG 173 (update April 2018) http://www.nice.org.uk/guidance/CG173

4. Review

Throughout NeP management patients should be reviewed regularly to optimise treatment. During these reviews the patient should be asked if the gabapentin/pregabalin prescribed has made a difference to the pain (Neuropathic Pain Scale) If the patient does not experience improved pain relief or if the pain has resolved consider stopping.

Current evidence suggests that the risk of misuse may be greater with pregabalin than gabapentin. Consider changing patients to gabapentin who have never previously tried gabapentin for NeP rather than continuing with pregabalin.

Community pain clinics promote exercise for NeP patient. These patients should be reviewed to consider stopping NeP prescribing once exercise eases the symptoms of pain.

Switching pregabalin to gabapentin in patients with normal renal function

Pregabalin is indicated for peripheral & central neuropathic pain and gabapentin for peripheral neuropathic pain. Beware of converting or switch these medications purely based on dosing (Reference CG173)

If switching is appropriate, this would be a straight switch, rather than titrating down the pregabalin dose and titrating up the gabapentin dose.

Pregabalin total daily dose pre-switch	**Gabapentin total daily dose post switch (Toth study[8])**	**Suggested daily dose of gabapentin**
150mg	900mg	300mg tds
225mg	901mg to 1500mg	400mg tds
300mg	1501mg to 2100mg	2x300mg tds
450mg	2101mg to 2700mg	2x400mg tds
600mg	2701mg to 3600mg	3x300mg tds

For daily doses of pregabalin below 150mg daily, e.g. 100mg, 75mg – switch to gabapentin 100mg tds, and titrate up if necessary.

Renal impairment: dose reductions are recommended for both pregabalin (CrCl<60ml/min) and gabapentin (CrCl< 80ml/min). If appropriate to switch, please also refer to www.medicines.org.uk for further information on recommended dose of gabapentin.

5. Discontinuing

The summary of product characteristics for gabapentin and pregabalin indicate that both drugs can be discontinued over one week. A more gradual dose taper allows observation of emergent symptoms that may have been controlled by the drug.

Pregabalin: reduce the daily dose at a maximum of 50-100mg/week.
Gabapentin: reduce the daily dose at a maximum rate of 300mg every four days.

Examples of withdrawal schedules

Example withdrawal schedule for a dose of Pregabalin 150mg bd

	Week 1	Week 2	Week 3	Week 4	
Morning	150mg	75mg	50mg	25mg	Stop and review Patient
Evening	75mg	75mg	50mg	25mg	

Example withdrawal schedule for a dose of Gabapentin 600mg TDS

	Week 1	Week 2	Week 3	Week 4 Review	Week 5	Week 6	Week 7
Morning	600mg	300mg	300mg	200mg	100mg	100mg	Stop and review patient
Midday	300mg	300mg	300mg	200mg	100mg		
Night	600mg	600mg	300mg	200mg	100mg	100mg	

References

1. An update on the drug treatment of neuropathic pain Part 1 DTB 2012; 50(10): 114-7
2. An update on the drug treatment of neuropathic pain Part 2 DTB 2012; 50(11): 126-9
3. Moore RA et al. Gabapentin for chronic neuropathic pain and neuralgia in adults. Cochrane database of systematic reviews 2009, Issue 3
4. Moore RA al. Pregabalin for acute and chronic pain in adults. Cochrane 2011, Issue3
5. NHS choices http://www.nhs.uk/medicine-guides/pages/MedicineSideEffects.aspx?condition=Neuropathic%20pain&medicine=pregabalin
6. eMC Neurontin /Lyrica SPC Accessed 29.12.14 at http://www.medicines.org.uk/emc/medicine/14651
7. UKMi Q&A 408.1 How do you switch between pregabalin and gabapentin for neuropathic pain, and vice versa? 2012 Accessed 29.12.14
8. Toth C Substitution of gabapentin therapy with pregabalin therapy in neuropathic pain due to peripheral neuropathy. Pain Medicine 2010; 11:456-465
9. NICE Clinical Guideline 66 The Management of Type 2 Diabetes http://www.nice.org.uk/nicemedia/pdf/CG66NICEGuideline.pdf
10. Public Health England. NHS England pregabalin and gabapentin advice Dec 2014 Accessed 14.5.15

Acknowledgements - Derbyshire medicines management and West Essex CCG.
http://www.derbyshiremedicinesmanagement.nhs.uk/assets/Clinical_Guidelines/Formulary_by_BNF_chapter_prescribing_guidelines/BNF_chapter_4/Neuropathic_Pain.pdf
http://www.westessexccg.nhs.uk/Downloads/Your%20NHS/Medicines%20optimisation/November%2013/Pregabalin%20switch%20document.pdf

APPROVAL PROCESS

Written by:	**CSU Medicines Management Team, Hull (dec 2014) Updated by Interface Pharmacist May 2015**
Consultation process:	**Hull Prescribing Subcommittee**
Approved by:	**MMIG**
Ratified by:	**HERPC Sep 15 Update Jan 19**
Review date:	**Jan 2022**

Appendix 1

Neuropathic pain scale

There are scales for measuring different aspects of pain. For one patient, a pain might feel extremely hot, but not at all dull, while another patient may not experience any heat, but feel like their pain is very dull. We expect you to rate very high on some of the scales below, and very low on others. We want you to use the measures that follow to tell us exactly what you experience.

1. Intensity of your pain. Answer:

No pain (0)

The most intense pain (10)

2. How sharp is your pain? Words used to describe "sharp" feelings include "like a knife," "like a spike," "jabbing" or "like jolts." **Answer:**

Not sharp (0)

The sharpest sensation imaginable 'like a knife' (10)

3. How hot does your pain feel? Words used to describe very hot pain include "burning" and "on fire." Answer:

Not hot (0)

The hottest sensation imaginable 'on fire' (10)

4. How dull does your pain feel? Words used to describe very dull pain include "like a dull toothache," "dull pain," and "like a bruise." Answer:

Not dull (0)

The most dull sensation imaginable (10)

5. How cold does your pain feels. Words used to describe very cold pain include "like ice" and "freezing." Answer:

Not cold (0)

The most cold sensation imaginable 'freezing' (10)

6. How sensitive does your skin to light touch or clothing. Words used to describe sensitive skin include "like sunburned skin" and "raw skin." Answer:

Not sensitive (0)

The most sensitive sensation Imaginable 'raw skin' (10)

7. How itchy does your pain feel? Words used to describe itchy pain include "like poison oak" and "like a mosquito bite." Answer:

Not itchy (0)

The itchiest sensation imaginable (10)

8. Which of the following best describes the time quality of your pain? Please tick only one answer.

( ) I feel a background pain all of the time and occasional flare-ups (break-through pain) some of the time.

Describe the background pain:

Describe the flare-up (break-through) pain:

( ) I feel a single type of pain all the time.

Describe this pain:

( ) I feel a single type of pain only sometimes. Other times, I am pain-free.

Describe this occasional pain:

9**. Now that you have told us the different physical aspects of your pain, the different types of sensations, we want you to tell use overall how unpleasant your pain is to you. Words used to describe very unpleasant pain include "miserable" and "intolerable." Remember, pain can have a low intensity, but still feel extremely unpleasant, and some kinds of pain can have a high intensity but be very tolerable. With this scale, please tell us how unpleasant your pain feels. Answer:**

Not unpleasant (0)

The most unpleasant sensation Imaginable 'intolerable' (10)

10. Lastly, we want you to give us an estimate the severity of your deep versus surface pain. We want you to rate each location of pain separately. We realise that it can be difficult to make these estimates, and most likely it will be a "best guess," but please give us your best estimate.

HOW INTENSIVE IS YOUR DEEP PAIN? Answer:

No deep pain (0)

The most intense deep pain sensation imaginable (10)

HOW INTENSIVE IS YOUR SURFACE PAIN? Answer:

No surface pain (0)

The most intense surface pain sensation imaginable (10)