Guidance for Review of Patients taking Pregabalin or Gabapentin 
for Neuropathic Pain in Primary Care

Aim

To review effectiveness of pregabalin or gabapentin in patients who have been taking it for more than 12 months for the treatment of neuropathic pain.

Background

Gabapentin and pregabalin are available as treatment options for neuropathic pain (2\textsuperscript{nd} and 3\textsuperscript{rd} line respectively after amitriptyline). Pregabalin has a similar mode of action to gabapentin and should only be used if gabapentin was effective but the patient did not tolerate the side effects.

After 6 to 12 months of use, the initial benefit that some patients may have obtained from gabapentin/pregabalin for the treatment of their neuropathic pain may no longer exist. Ipswich Hospital’s Pain Specialists therefore support the principle of the gradual trial withdrawal of gabapentin/pregabalin in appropriate patients after a period of 12 months, to assess whether the medication continues to provide a significant benefit.

Gabapentin and pregabalin are only licensed for neuropathic pain; there is little evidence to support the use of these medicines for non-neuropathic pain conditions. Prescribers should consider interventions more likely to help the patient such as physical rehabilitation for back pain and musculoskeletal pain.

Note: Gabapentin and pregabalin are liable to misuse, diversion and can cause dependence. Both gabapentin and pregabalin have adverse effects on the central nervous system, which are additive when used with other centrally acting drugs, particularly opioids. The pharmacokinetic properties of pregabalin make the drug relatively more dangerous than gabapentin in high doses (PHE/NHSE 2014).

Review Process

1. Identify patients taking gabapentin or pregabalin for neuropathic pain for longer than 12 months.
2. Obtain relevant information from patient notes to support potential review (see Appendix 1).
3. Select patients considered as potential candidates for trial withdrawal.
4. Invite patients in for review (Sample patient letter attached in Appendix 2).
5. Complete the PAIN DETECT questionnaire (Appendix 3) as a baseline assessment as part of the initial review. (Consider asking the patients to complete the PAIN DETECT questionnaire themselves in advance and bring to the review).

Scenario One: If the pain score is LOW at time of review (i.e. pain well controlled):

i. Provide patient with dosage reduction instructions. A blank patient dosage instruction form can be found in Appendix 4.
**Pregabalin:**

A suggested dosage reduction regime is to reduce 25-30% every week. Reduction should not exceed 50-100mg at any step. E.g. Pregabalin 300mg bd dose reduction schedule would be:

<table>
<thead>
<tr>
<th>Starting Dose</th>
<th>Week 1</th>
<th>Week 2</th>
<th>Week 3</th>
<th>Week 4</th>
<th>Week 5</th>
<th>Week 6</th>
<th>Week 7</th>
<th>Week 8</th>
<th>Week 9</th>
<th>Week 10</th>
<th>Week 11</th>
</tr>
</thead>
<tbody>
<tr>
<td>AM</td>
<td>300mg</td>
<td>300mg</td>
<td>200mg</td>
<td>200mg</td>
<td>150mg</td>
<td>100mg</td>
<td>100mg</td>
<td>50mg</td>
<td>50mg</td>
<td>25mg</td>
<td>25mg</td>
</tr>
<tr>
<td>PM</td>
<td>300mg</td>
<td>200mg</td>
<td>200mg</td>
<td>100mg</td>
<td>100mg</td>
<td>50mg</td>
<td>50mg</td>
<td>25mg</td>
<td>25mg</td>
<td></td>
<td>STOP and review patient</td>
</tr>
</tbody>
</table>

**Gabapentin:**

A suggested dosage reduction regime is to reduce by 300mg every 4 days. E.g. Gabapentin 1.2g TDS dose reduction schedule would be:

**Dosage Reduction Guidance**

<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Morning</td>
<td>1200mg</td>
<td>1200mg</td>
<td>1200mg</td>
<td>900mg</td>
<td>900mg</td>
<td>600mg</td>
<td>600mg</td>
<td>600mg</td>
<td>300mg</td>
<td>300mg</td>
<td>300mg</td>
<td>STOP and review patient</td>
</tr>
<tr>
<td>Lunch</td>
<td>1200mg</td>
<td>1200mg</td>
<td>900mg</td>
<td>900mg</td>
<td>600mg</td>
<td>600mg</td>
<td>600mg</td>
<td>300mg</td>
<td>300mg</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Dinner</td>
<td>1200mg</td>
<td>900mg</td>
<td>900mg</td>
<td>900mg</td>
<td>600mg</td>
<td>600mg</td>
<td>300mg</td>
<td>300mg</td>
<td>300mg</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
ii. Give patient a blank PAIN DETECT questionnaire to complete at the end of the dosage reduction period.

iii. Invite patient back for review at end of trial withdrawal or sooner if experiencing problems

iv. Complete Patient Review Summary Form (Appendix 1) to as part of summary of outcomes of all patient trial withdrawals.

Scenario Two: If pain score is HIGH at time of review (i.e. pain is not well controlled) and PAIN DETECT questionnaire confirms pain is neuropathic in nature

i. Consider additional/change in neuropathic agent (see appendix 5 for treatment options) or,

ii. Refer to Secondary Care Pain Clinic if:
   • Patient’s symptoms are unresponsive to treatment and an acceptable reduction in pain is not achieved
   • There is response to treatment but unacceptable side-effects and all options have been considered
   • Bio-psychosocial needs and difficulty in coping (“yellow flags”)
   • Further advice or diagnosis is needed on the particular clinical symptom set

Scenario Three: If pain does not appear to be neuropathic in nature and is not currently well controlled – consider a change of treatment as gabapentin and pregabalin are only licensed for neuropathic pain.

Appendices:
Appendix 1: Data collection form
Appendix 2: Sample patient letter
Appendix 3: Diagnostic screening tool - Pain Detect questionnaire
Appendix 4: Dose reduction instructions for patients
Appendix 5: Guidelines for the Management of Neuropathic Pain in Primary Care

References:
Appendix 1: Data collection form

<table>
<thead>
<tr>
<th>Patient identifier</th>
<th>DOB</th>
<th>PAST &amp; CURRENT TREATMENT DETAILS</th>
<th>OUTCOME OF INITIAL REVIEW</th>
<th>OUTCOME OF FOLLOW UP REVIEW</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Drug</td>
<td>Strength and dose</td>
<td>Indication</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Appendix 2: Example patient letter

Dear ...

We are currently undertaking a review of patients at the GP Practice who are taking medication to treat “nerve pain”.

We notice from your records that you have been taking pregabalin/gabapentin (delete as appropriate) for some time now and may benefit from a review. We may be able to reduce your pain medication if your pain is well controlled, or review it to another medication/change your dose if the pain is not well controlled. Ipswich Hospital’s Pain Specialists support this work.

We would like to invite you to attend the GP practice to discuss this with you. Please could you phone the surgery to book an appointment. Prior to seeing you, it would be useful if you could complete the enclosed questionnaire, so that we can assess how well your pain is being controlled on your current medication.

Yours sincerely,
Appendix 3: Useful links

- The PAIN DETECT Questionnaire
  The neuropathic pain assessment tool can be found at:

- Pregabalin and Gabapentin: advice for prescribers on the risk of misuse

- Pain Toolkit
  https://www.paintoolkit.org/persistent-pain/the-pain-cycle

- Tame the Beast: How to rethink persistent pain
  https://www.tamethebeast.org/

- Driving and Pain

- Turning Point
  http://turning-point.co.uk/suffolk-recovery-network-ipswich.aspx

- Wellbeing Service
  https://www.wellbeingnands.co.uk/
Appendix 4:

Pregabalin for neuropathic pain – dosage reduction instructions for patient

<table>
<thead>
<tr>
<th>Starting Dose</th>
<th>Week 1</th>
<th>Week 2</th>
<th>Week 3</th>
<th>Week 4</th>
<th>Week 5</th>
<th>Week 6</th>
<th>Week 7</th>
<th>Week 8</th>
<th>Week 9</th>
<th>Week 10</th>
<th>Week 11</th>
<th>Week 12</th>
</tr>
</thead>
<tbody>
<tr>
<td>AM</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>PM</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Gabapentin: for neuropathic pain – dosage reduction instructions for patient

<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Morning</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lunch</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Dinner</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Please attend the GP practice for a further review once the above dosage reduction is complete, or sooner if you experience any problems or worsening pain.

It would be useful if you kept a symptom diary over the dosage reduction period, including details of activities undertaken, ability to work and drive, quality of sleep and general mood (e.g. depression/anxiety) and the associated pain experienced.

Please also complete the PAIN DETECT Questionnaire again at the end of the dosage reduction period and bring it with you to the follow up review.
Appendix 5:

**Guidelines for the Management of Neuropathic Pain in Primary Care**

Neuropathic pain is caused by abnormally damaged nerves. Possible causes include nerve damage due to trauma or conditions such as diabetes, herpes zoster (shingles) and trigeminal neuralgia. Neuropathic pain may be considered in ongoing conditions e.g. sciatica, neck pain and low back pain. It may also be a feature of underlying conditions e.g. malignancy, that require investigation.

Neuropathic pain may present as:

- **Dysesthesia** - an unpleasant, abnormal sensation
- **Hyperalgesia** - increased sensitivity to normal pain stimulus e.g. temperature
- **Allodynia** - pain caused by a stimulus that does not normally produce pain – e.g. wearing clothes
- **Motor-dystonia**, weakness and paralysis, fasciculations
- **Autonomic signs including skin changes such as shininess, oedema, change of perspiration**

Neuropathic pain may be spontaneous or evoked, continuous or intermittent and is often worse at the end of the day. Patients’ descriptors of the pain include: shooting, tingling, burning, sharp, nagging, electric shock.

2-4% of the general population is thought to be affected by neuropathic pain. Adequate assessment and accurate diagnosis is essential for specific treatment options to be considered. Diagnostic screening tools can be useful such as PAIN DETECT.

All treatment strategies need to be individualised to specific patient requirements and tolerance. Patients beliefs and perception of the pain and its cause, disturbed sleep, anxiety, mood changes and coping strategies will also need to be addressed and treating anxiety or depression first may reduce the need for analgesics.

Consider non-pharmacological elements to the management e.g. address physical and emotional aspects, as well as pain, by encouraging physical activity, improving poor sleep.

**Pharmacological interventions should be increased to full therapeutic and tolerated dose before switching or adding a different agent.**

Realistic goals need to be set – pain free status is not usually achievable and 20-50% reduction in pain is a commonly used end-point in clinical trials.

If complex regional pain syndrome is suspected, refer urgently to Pain clinic, since there is a window of opportunity to treat this before it becomes chronic and untreatable.

Please note: these guidelines are not intended to cover Palliative Care.
Treatment options

- Treatment review at 2, 4 and 8 weeks is recommended to assess effectiveness of the neuromodulatory medication. However, the median effective dose should have been achieved at 8 weeks to assess accurately i.e. amitriptyline 25-50mg on, gabapentin 600mg tds; or pregabalin 150mg bd.

- If the drug is effective, continue for 12 MONTHS and then consider dosage reduction and trial withdrawal to assess continuing benefit being obtained, if any.

- Start treatment at a low dose (see schedules below) and slowly titrate up if required and tolerated by the patient

Key

Green: £3 - £12 / month
Amber: £13 - £30 / month
Red: >£60 / month

<table>
<thead>
<tr>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Night</td>
</tr>
<tr>
<td></td>
<td>10mg</td>
</tr>
</tbody>
</table>

- Take at night to reduce hangover effect and to promote sleep.
- Patients should be encouraged to persist with treatment as tolerance to side-effects is possible
- The usual maximum dose is 50mg once daily
- Titrate down slowly if stopping therapy
- Avoid co-prescribing of tramadol as increases risk of CNS toxicity
- Risk of antimuscarinic and CNS side effects – caution in elderly patients

<table>
<thead>
<tr>
<th>Second line</th>
<th>Imipramine [unlicensed indication] – Only if amitriptyline is effective but not well tolerated due to side effects.</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Night</td>
</tr>
<tr>
<td></td>
<td>10mg</td>
</tr>
</tbody>
</table>

- Take at night to reduce hangover effect and to promote sleep.
- Slowly increase dose if pain relief insufficient and patient tolerating treatment. Patients should be encouraged to persist with treatment as tolerance to side-effects is possible
- The usual maximum dose is 50mg once daily
- Titrate down slowly if stopping therapy
- Avoid co-prescribing of tramadol as increases risk of CNS toxicity
- Risk of antimuscarinic and CNS side effects – caution in elderly patients
### Gabapentin

<table>
<thead>
<tr>
<th></th>
<th>Day 1</th>
<th>Day 2</th>
<th>Day 3 - 7</th>
<th>Day 8 - 9</th>
<th>Day 10-11</th>
<th>Day 12</th>
</tr>
</thead>
<tbody>
<tr>
<td>Morning</td>
<td>300mg</td>
<td>300mg</td>
<td>300mg</td>
<td>600mg</td>
<td>600mg</td>
<td>600mg</td>
</tr>
<tr>
<td>Midday</td>
<td>300mg</td>
<td>300mg</td>
<td>300mg</td>
<td>300mg</td>
<td>600mg</td>
<td>600mg</td>
</tr>
<tr>
<td>Night</td>
<td>300mg</td>
<td>300mg</td>
<td>300mg</td>
<td>600mg</td>
<td>600mg</td>
<td>600mg</td>
</tr>
</tbody>
</table>

- Titrate dose by 300mg every 2-3 days to maximum of 1200mg tds as required.
- May need to wait for up to 2 weeks to experience maximal benefits.
- Titrate down slowly if stopping therapy.
- Advise patient and carer(s) of possible drowsiness and effect on driving
- Caution: Gabapentin – risk of dependence, misuse and diversion.

### Duloxetine

- Initiate on 60mg at night. If side effects occur consider dose reduction
- Licensed for diabetic peripheral neuropathic pain only; unlicensed for other types of neuropathic pain
- Response is seen within ONE WEEK.
- Discontinue if inadequate response after 2 months
- On-going treatment should be reviewed on a regular basis every 3 months
- The maximum dose is 120 mg per day.
- Titrate down slowly if stopping therapy (over a period of at least 1-2 weeks)

### Pregabalin – Only if gabapentin is effective but not well tolerated due to side effects.

<table>
<thead>
<tr>
<th></th>
<th>Week 1</th>
<th>Week 2</th>
<th>Week 3</th>
</tr>
</thead>
<tbody>
<tr>
<td>Morning</td>
<td>75mg</td>
<td>150mg</td>
<td>300mg</td>
</tr>
<tr>
<td>Evening</td>
<td>75mg</td>
<td>150mg</td>
<td>300mg</td>
</tr>
</tbody>
</table>

- If required doses can be increased after 3-7 days to a maximum dose of 300mg bd
- Always prescribe as BD dosing (more cost effective than TDS)
- Elderly patients may require a dose reduction of pregabalin due to a decreased renal function (see SPC for more details)
- Caution: Pregabalin – risk of dependence, misuse and diversion.

### Capsaicin 0.075% cream (Axsain®)

- Consider for people with localised neuropathic pain who wish to avoid, or who cannot tolerate, oral treatments.
- Treatment of painful diabetic peripheral polyneuropathy using capsaicin cream should be under the direct supervision of a hospital consultant who has access to specialist resources.
- The recommended duration of use is **8 weeks**, then refer for consultant assessment

If above treatments are not effective:

- Refer to a specialist pain service and/or a condition-specific service
  - Consider tramadol only if acute rescue therapy is needed while waiting for referral. Tramadol should not be continued long-term without specialist advice.
The combination of tramadol with amitriptyline, imipramine, or duloxetine is associated with a low risk of serotonin syndrome (the features of which include confusion, delirium, shivering, sweating, changes in blood pressure and myoclonus).

- Do not start treatment with strong opioids (such as morphine or oxycodone) without an assessment by a specialist pain service or a condition-specific service.

Nb. Lidocaine patches should only be initiated by a pain or palliative care specialist consultant for localised neuropathic pain (scar pain, post herpetic neuralgia). The consultant must provide the first 4 weeks of treatment and confirm that the patches are effective for the patient before prescribing may move to primary care. The consultant must complete a proforma to confirm this and send it to the GP to move prescribing to primary care. Lidocaine patches should be reviewed by the prescriber for on-going effectiveness every 3 months.