GMMMG
Greater Manchester
Medicines Management Group

# Neuropathic Pain Guideline

Seeking to
identify and champion
the appropriate use of drugs
across Greater Manchester

NHS

# Document Control

Revision History:

The latest version will be held on the GMMMG website.

| Date | Actioned by | Comments/Summary of changes | Version |
|---|---|---|---|
| 11.12.2013 | B Reddy, Regional Drug and Therapeutics Centre www.rdtc.nhs.uk | Draft Written | V01 |
| 23.12.2013 | B Reddy | Updated following comments received at GMMMG. | V02 |
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Approval:

This document must be approved by the following before distribution:

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| **GMMMG** | Neuropathic Pain Guideline | 20.03.14 | V05 |

# Foreword

Neuropathic pain is managed in many patients by the use of simple assessment scales of the pain itself, a review of both physical and psychological functional impairment and pharmacological and non-pharmacological treatments, coupled with an idea of the patient's goals/expectations for the management of his/her pain. Some patients who suffer from pain that does not respond to standard therapies may require a more in-depth assessment and will need to be referred to secondary care.

One of the aims of this document is to aid with differentiating those patients who can be managed very successfully in primary care and those who require the more complex involvement of healthcare professionals in secondary care. Many patients who are already within a secondary care setting but go on to develop neuropathic pain (whilst under another speciality e.g. orthopaedics) are often referred directly to pain clinics when they can be managed quite effectively by primary care in the first instance.

This document has been developed utilising the latest clinical evidence but adapting it to include treatments based on clinical experience whilst also considering the best use of scarce NHS resources for the whole GM population.

Whilst this guideline is primarily for primary care, we would expect the same principles to apply in a secondary care setting also.

GMMMG
March 2014.

# AIM

To promote the rational use of analgesics, and associated adjuvant treatment, so that neuropathic pain is optimally managed in a patient.

Implementation of the following guidance aims to improve the safe and effective use of treatments for the symptomatic relief of neuropathic pain.

This guideline is based on the *Neuropathic Pain –The pharmacological management of neuropathic pain in adults in non-specialist settings NICE CG 173 (Nov 13)* with some local adaptation.

# GUIDELINE

## 1. Introduction

1.1 The International Association for the Study of Pain (IASP 2011) defines neuropathic pain as 'pain caused by a lesion or disease of the somatosensory nervous system'. Central neuropathic pain is defined as 'pain caused by a lesion or disease of the central somatosensory nervous system', and peripheral neuropathic pain is defined as 'pain caused by a lesion or disease of the peripheral somatosensory nervous system'.

1.2 Neuropathic pain is very challenging to manage because of the heterogeneity of its aetiologies, symptoms and underlying mechanisms. There is often uncertainty regarding the nature and exact location of a lesion or health condition associated with neuropathic pain, particularly in non-specialist settings.

1.3 Examples of common conditions that have peripheral neuropathic pain as a symptom are painful diabetic neuropathy, post-herpetic neuralgia, trigeminal neuralgia, radicular pain, post-surgical chronic neuropathic pain, and neuropathic cancer pain (such as, chemotherapy-induced neuropathy, neuropathy secondary to tumour antigens, or caused by direct invasion or compression of neural structures). Examples of conditions that can cause central neuropathic pain include stroke, spinal cord injury and multiple sclerosis.

1.4 Neuropathic pain can be intermittent or constant, and spontaneous or provoked. Typical descriptions of the pain include terms such as shooting, stabbing, like an electric shock, burning, tingling, tight, numb, prickling, and itching and a sensation of pins and needles.

1.5 Neuropathic pain is thought to affect 2 - 4% of the general population. 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. **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.** See information for patients section for example leaflets that are available that could be used to aid these discussions.

1.6 Screening tools can be useful to aid diagnosis: the Neuropathic Pain Scale (NPS) is a well-known validated scale (see appendix 1). Evidence supports the validity of the NPS for detecting change in pain after treatments; however other pain scales are available.

**1.7 For all drugs, recommendations are based on evidence of clinical and cost effectiveness and reflect whether their use for the management of neuropathic pain is a good use of NHS resources.**

## 2. **Key Principles of Care**

2.1 When agreeing a treatment plan with the person, take into account their concerns and expectations, and discuss:

- the severity of the pain, and its impact on lifestyle, daily activities (including sleep disturbance) and participation
- the underlying cause of the pain and whether this condition has deteriorated
- why a particular pharmacological treatment is being offered
- the benefits and possible adverse effects of pharmacological treatments, taking into account any physical or psychological problems, and concurrent medications
- The importance of dosage titration and the titration process, providing the person with individualised information and advice
- Setting realistic expectations of treatment. Achieving pain free status may not be achievable. Clinical trials use a pain reduction score of 50%
- Coping strategies for pain and for possible adverse effects of treatment
- Non-pharmacological treatments, for example, physical and psychological therapies (which may be offered through a rehabilitation service) and surgery (which may be offered through specialist services).

2.2 Consider referring the person to a specialist pain service and/or a condition specific Service at any stage, including at initial presentation and at the regular clinical reviews if:

- No significant improvement after at least three months of treatment
- Their underlying health condition has deteriorated or
- they have severe pain or
- their pain significantly limits their lifestyle, daily activities (including sleep disturbance) and participation.

***It is important that patient's expectations are realistic when considering the management of their pain. Achieving pain free status is not always achievable, <u>despite</u> referral to the pain clinic.***

2.3 Carry out regular clinical reviews to assess and monitor the effectiveness of the treatment. Each review should include an assessment of:

- pain control
- impact on lifestyle, daily activities (including sleep disturbance) and participation
- physical and psychological wellbeing
- adverse effects
- Continued need for treatment.

2.4 After starting or changing a treatment, carry out an early clinical review of dosage titration, tolerability and adverse effects to assess the suitability of the chosen treatment.

2.5 All treatments should be titrated appropriately and given for an adequate duration prior to moving to the next option.

# 3. Pharmacological Treatment

Please note that this information is a summary to guide prescribers – for further information please consult individual SPC's at www.medicines.org.uk

## 3.1 All neuropathic pain (except trigeminal neuralgia)

Many products are not specifically licensed for neuropathic pain and it is important to advise patients of this.

3.1.1 Offer patients amitriptyline first line. Analgesic effect of amitriptyline is separate from its antidepressant effect.

- It is best taken in the evening to reduce 'hangover effect' e.g. 6-8pm
- Slowly titrate to reduce side-effects but ensure titration occurs even if dose is later reduced.
- A typical dosage regimen may be as below:

    - Step 1 Amitriptyline 10mg at night* for 2 weeks
    - Step 2 Amitriptyline 20mg at night* for 6 weeks
    - Step 3 Amitriptyline 30mg at night*
    - Step 4 Amitriptyline 40mg at night*
    - Step 5 Amitriptyline 50mg at night*

    * Ensure patient tolerates dose at each step before increasing dose.

- After step 2 the dose can be increased gradually according to tolerance and the patient's needs.
- The normal maximum dose is 50mg daily but up to 100mg can be used if the patient is deriving benefit with limited side-effects
- Side-effect profiles are similar but alternative TCAs e.g. Imipramine or nortriptyline may be used if amitriptyline is not well tolerated.
- If amitriptyline is not tolerated it should be withdrawn gradually over 1-2 weeks.

3.1.2 If the maximum dose of amitriptyline (or alternatives) is unsuccessful in controlling pain then the patient should be switched to Gabapentin, titrating the dose gradually to prevent adverse effects, until effective pain relief is achieved.

- Various dose titrations may be used for gabapentin, depending on the person taking it and how well they tolerate it. The speed of titration will vary among individuals and should be tailored to the individual; if the person is elderly or frail they are more likely to experience adverse effects and will require slower titration. The dose should be adjusted for renal impairment.
- It may take several weeks to reach an effective dosage (usually 1200 mg to 3600 mg daily). Onset of action may be seen as early as the second week of treatment with rapid titration, but the peak effect usually occurs about 2 weeks after a therapeutic dosage is achieved (therefore an adequate trial may be 2 months or longer).
- Consider trialling gabapentin for 3–8 weeks, with at least 2 weeks at the maximum tolerated dose, before deciding it is not effective.
- Gabapentin should be discontinued gradually over a minimum of 1 week.

3.1.3 Pregabalin is only appropriate if gabapentin is effective but not tolerated due to side effects. A fully documented trial of pregabalin (75mg – 300mg/day for 8 weeks) may be considered in patients who cannot tolerate gabapentin or who have not responded fully despite an adequate trial.

3.1.4 Reports of recreational abuse of pregabalin and gabapentin have been around for some time. This is something that should be considered when prescribing either pregabalin or gabapentin and prescribers must evaluate choice of agent based on whether the patient has a history of substance misuse. Duloxetine may be used, higher up the treatment pathway in a prison setting for this reason. It has been noted that it appears easier to achieve a recreational high with pregabalin rather than gabapentin; in addition new emerging reports suggest that pregabalin given in combination with alcohol or other street drugs appears to enhance the recreational high of alcohol and/or other drugs.

3.1.5 If there is a partial response to either amitriptyline (or alternative) or gabapentin (or alternative) then amitriptyline and gabapentin in combination should be tried.

3.1.6 Duloxetine may be considered as an option where other treatments have failed or for a clear diagnosis of diabetic neuropathy.

- Start at 60 mg per day.
- A lower starting dose of 30mg may be appropriate for some people (for example, if tolerability is a problem).
- Titrate upward to an effective dose or the person's maximum tolerated dose of no higher than 120 mg per day.

3.1.7 Consider tramadol **only** if acute rescue therapy is needed

*Prescribers are reminded that tramadol is a schedule 3 CD due to increases in the numbers of deaths relating to its misuse over the last few years.*
***NB Tramadol is not recommended for long term use.***

3.1.8 Consider capsaicin cream (starting at 0.025% pea size amount four times/day for 6-8 weeks) for people with localised neuropathic pain who wish to avoid, or who cannot tolerate oral treatments.

3.1.9 When the pain is in remission, reduce the dosage and gradually withdraw the drug if the person remains pain-free for 1 month.

## 3.2 Trigeminal neuralgia

3.2.1 Offer carbamazepine as initial treatment for trigeminal neuralgia.

- Start at 100 mg twice daily and titrate the dosage up until pain is relieved (for example increase by a maximum of 100 mg every 3 days, according to tolerability and efficacy).
- In the majority of people a dosage of 200 mg three or four times a day is sufficient to prevent paroxysms of pain (maximum dosage 1600 mg daily).
- Modified release preparations may be useful at night if the person experiences breakthrough pain

3.2.2 If initial treatment with carbamazepine is not effective, is not tolerated or is contraindicated, consider gabapentin.

- Start at 300 mg on day 1, and then increase to 300 mg twice a day on day 2, then to 300 mg three times a day on day 3. After this, based on individual response and tolerability, increase in increments of 300 mg per day every 2–3 days up to a maximum dosage of 3600 mg daily.
- A lower starting dosage and slower titration regimens may be appropriate for some people, particularly the elderly or those with renal impairment.
- Consider trialling gabapentin for 3–8 weeks, with at least 2 weeks at the maximum tolerated dosage, before deciding it is not effective.

3.2.3 When the pain is in remission, reduce the dosage and gradually withdraw the drug if the person remains pain-free for 1 month.

3.2.4 If pain is not sufficiently relieved, seek specialist advice or refer to a specialist in pain management or a neurologist.

## 4. Treatments not supported for use (as per NICE Guideline)

4.1 The following treatments should not be routinely prescribed for the treatment of neuropathic pain unless advised by a specialist to do so (but see points 4.5 and 4.6 below)

- **cannabis sativa extract**
- **capsaicin patch**
- **lacosamide**
- **lamotrigine**
- **levetiracetam**
- **morphine**
- **oxycodone**
- **oxcarbazepine**
- **topiramate**
- **tramadol (long-term use)**
- **Venlafaxine.**

4.2 NICE guidance states that the health economic model provided no support for the use of the above treatments. In all analyses, these treatments were dominated by a number of other alternatives and, in some cases, they were dominated by placebo (that is, they were predicted to have higher costs and lower net health gains than treatment with placebo).

4.3 Some of the listed treatments (lacosamide, levetiracetam, oxycodone and venlafaxine) do not appear to be more effective than placebo or there is a lack of evidence and/or inconsistent evidence about whether they are better than placebo at reducing pain.

4.4 Lidocaine patches are currently only licensed for use post-herpatic neuralgia. **The current GMMMG New Therapies recommendation does not recommend use for this indication or other off label (e.g. neuropathic pain) indications.** NICE guidance also could not recommend the use of lidocaine patches in neuropathic pain as there is an absence of cost effectiveness data.

4.5 Whilst the above list applies primarily to primary care; it is important to note that there is an absence of any positive evidence of efficacy for use of these drugs in neuropathic pain. They should therefore be reserved for use after other standard treatments have failed. If any of the treatments discussed above are used in a specialist setting then there should be clear documentation of benefit for that individual patient prior to continuing therapy.

4.6 If clear evidence of continuing benefit (e.g. A reduction in the neuropathic pain scale) for the patient is not supplied to primary care then secondary care will be expected to continue prescribing until such information can be supplied.

# Algorithm for management of Neuropathic Pain

Neuropathic Pain

Consider Capsaicin cream starting at 0.025% pea size amount four times a day for 6-8 weeks or increasing to 0.075% qds for 6-8 weeks (if tolerated but treatment suboptimal) for people with localised neuropathic pain who wish to avoid or cannot tolerate oral treatments.

**1st Line:** Amitriptyline: 10-50mg for 6-8 weeks. Normal dose = 50mg but up to 100mg can be used if the patient is deriving benefit with limited side effects.
If adverse effects consider: imipramine or nortriptyline.

Amitriptyline is best taken in the evening to reduce hangover effect e.g. 6-8pm. Slowly titrate to reduce side effects but ensure that titration occurs even if the dose is later reduced.
**If treatment is ineffective stop and consider:**

**2nd line:** Gabapentin: 1200mg-3600mg/day for 3-8 weeks. An adequate trial should include at least 2 weeks at the maximum tolerated dose before deciding it is ineffective.
If **adverse effects** consider: pregabalin 75mg to max of 300mg/day for 8 weeks.

Various dose titrations may be used for gabapentin and the speed of titration should be tailored to the individual. Elderly frail patients are more likely to experience side effects and therefore benefit from a slower titration.
Reports of recreational abuse of both gabapentin and pregabalin are increasing and history of substance misuse needs to be considered on initiation of treatment.

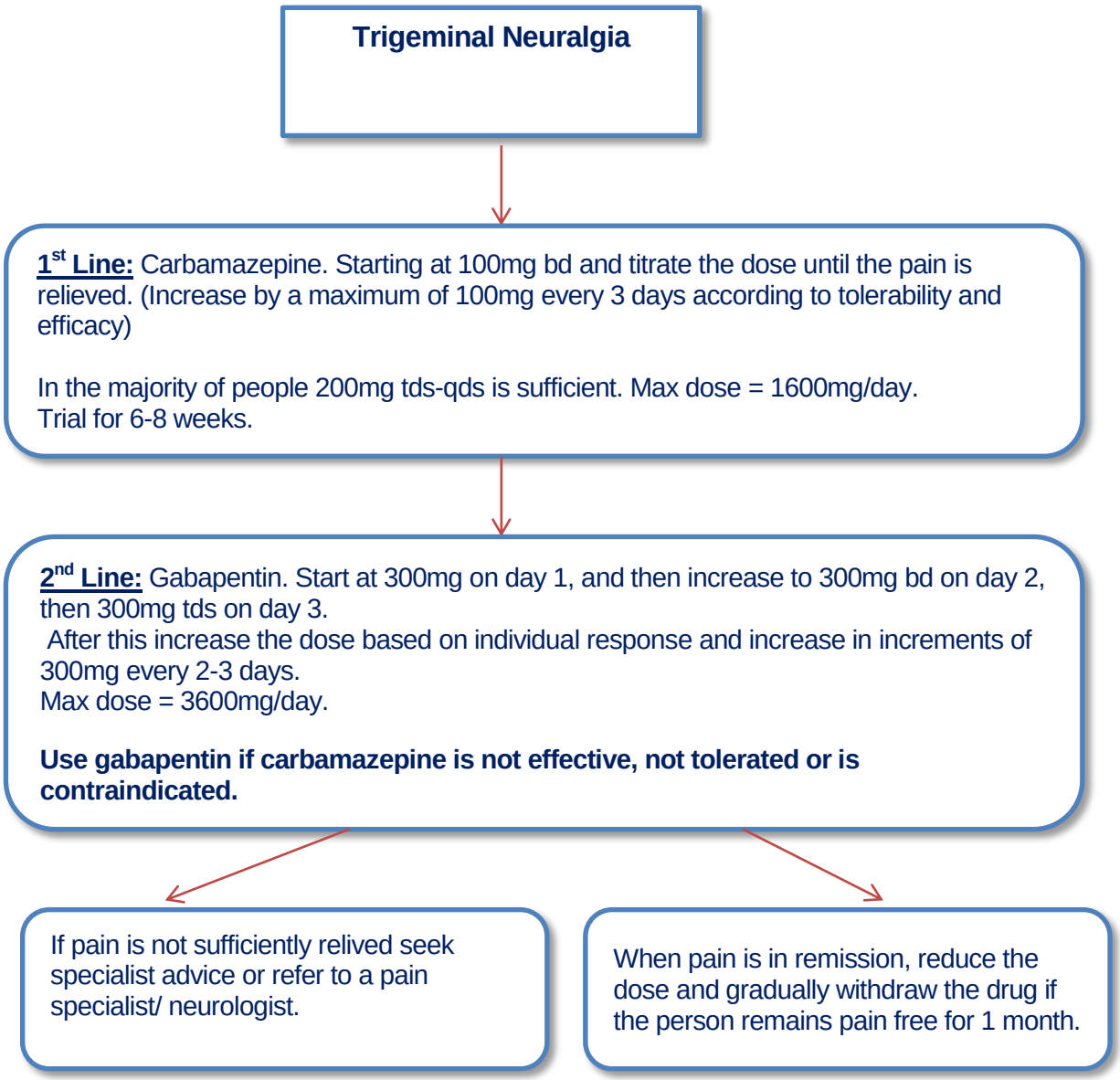
**3rd line:** If there is a partial response to either amitriptyline (or alternative) or gabapentin (or alternative) then amitriptyline in combination should be tried.
**If treatment is ineffective stop and consider:**

**4th line:** Duloxetine 30mg – 120mg/day titrated slowly.
Duloxetine may be considered as an option where other treatments have failed or for use **2nd line** for patients with a clear diagnosis of diabetic neuropathy.
Duloxetine may also be an option in patients with a history of substance misuse, particularly in a prison setting.

Consider tramadol ONLY if acute rescue therapy is needed. Should only be given for a short treatment duration and then stopped. Long term use not recommended.

When the pain is in remission, reduce the dosage and gradually withdraw the drug if the person remains pain free for 1 month.

# Algorithm for management of Trigeminal Neuralgia



## 5. Information for Patients

### Information leaflets

The British Pain Society: Understanding and managing pain information for patients
http://www.britishpainsociety.org/book_understanding_pain.pdf

Pain Concern: Information on use of amitriptyline for neuropathic pain
http://painconcern.org.uk/amitriptyline/

Pain concern: a guide to managing pain
http://painconcern.org.uk/wp-content/uploads/2013/08/Managing-Pain.pdf

The pain toolkit for people who live with persistent pain.
http://www.paintoolkit.org/assets/downloads/Pain-Toolkit-Booklet-Nov-2012.pdf

### Website links

The British Pain Society
Find answers to frequently asked questions and patient publications
www.britishpainsociety.org

Pain UK
Find out about other organisations helping people living with pain.
www.painuk.org

Living with Chronic Pain, by Neil Berry.
Listen to self-management tips in a free download or purchase on CD.
www.paincd.org.uk

Pain Relief Foundation
Find information, articles and CDs for purchase.
www.painrelieffoundation.org.uk

Pain Toolkit
Access the illustrated booklet and other useful tools for managing pain.
www.paintoolkit.org

## 6. References


1. National Institute for Health and Care Excellence (2013) [Neuropathic pain – pharmacological management: The pharmacological management of neuropathic pain in adults in non-specialist settings]. [CG173]. London: National Institute for Health and Care Excellence. http://publications.nice.org.uk/neuropathic-pain-pharmacological-management-cg173. Accessed December 11th 2013.

2. Clinical Knowledge Summaries: Neuropathic Pain – drug management http://cks.nice.org.uk/neuropathic-pain-drug-treatment#!scenariorecommendation:1 accessed December 20th 2013.

3. Clinical Knowledge Summaries: Trigeminal Neuralgia – Treatment http://cks.nice.org.uk/trigeminal-neuralgia#!scenariorecommendation. Accessed December 20th 2013

4. GMMMG previous neuropathic pain guidance – issued July 2010.

5. Safer Prescribing in Prisons: Guidance for Clinicians – RCGP secure environments group (November 2011)

6. IPNTS recommendation (September 2013): Lidocaine plasters http://www.nyrdtc.nhs.uk/GMMMG/Groups/Publications/IPNTS_docs/IPNTS_recom_2/IPNTS%20Lidocaine%20patches.pdf. Accessed December 10th 2013.

## 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. Please use the scale below to tell us how intense your pain is. Place an "X" through the number that best describes the intensity of your pain.

| 0 | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 |
|---|---|---|---|---|---|---|---|---|---|---|

No pain — The most intense pain sensation imaginable

2. Please use the scale below to tell us how sharp your pain feels. Words used to describe "sharp" feelings include "like a knife," "like a spike," "jabbing" or "like jolts."

| 0 | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 |
|---|---|---|---|---|---|---|---|---|---|---|

Not sharp — The sharpest sensation imaginable ('like a knife')

3. Please use the scale below to tell us how hot your pain feels. Words used to describe very hot pain include "burning" and "on fire."

| 0 | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 |
|---|---|---|---|---|---|---|---|---|---|---|

Not hot — The hottest sensation imaginable ('on fire')

4. Please use the scale below to tell us how dull your pain feels. Words used to describe very dull pain include "like a dull toothache," "dull pain," and "like a bruise."

| 0 | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 |
|---|---|---|---|---|---|---|---|---|---|---|

Not dull — The most dull sensation imaginable

5. Please use the scale below to tell us how cold your pain feels. Words used to describe very cold pain include "like ice" and "freezing."

| 0 | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 |
|---|---|---|---|---|---|---|---|---|---|---|

Not cold — The most cold sensation

imaginable
('freezing')

6. Please use the scale below to tell us how sensitive your skin is to light touch or clothing. Words used to describe sensitive skin include "like sunburned skin" and "raw skin."

| 0 | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 |
|---|---|---|---|---|---|---|---|---|---|---|

Not sensitive

The most sensitive sensation imaginable ('raw skin'

7. Please use the scale below to tell us how itchy your pain feels. Words used to describe itchy pain include "like poison oak" and "like a mosquito bite."

| 0 | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 |
|---|---|---|---|---|---|---|---|---|---|---|

Not itchy

The itchiest sensation imaginable

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. Works 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.

| 0 | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 |
|---|---|---|---|---|---|---|---|---|---|---|

Not unpleasant

The most unpleasant sensation Imaginable ('intolerable')

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?

| 0 | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 |
|---|---|---|---|---|---|---|---|---|---|---|

No deep pain

The most intense deep pain sensation imaginable

HOW INTENSIVE IS YOUR SURFACE PAIN?

| 0 | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 |
|---|---|---|---|---|---|---|---|---|---|---|

No surface pain

The most intense surface pain sensation imaginable