



GUIDELINES

ON THE MANAGEMENT OF

NEUROPATHIC PAIN

February 2008

These CREST guidelines have been produced by a sub-group of health care professionals chaired by Dr Pamela Bell.

The Clinical Resource Efficiency Support Team (CREST) is a small team of health care professionals established under the auspices of the Central Medical Advisory Committee in 1988. The aims of CREST are to promote clinical efficiency in the Health Service in Northern Ireland, while ensuring the highest possible standard of clinical practice is maintained.

CREST is currently amalgating with the Regional Multi-professional Audit Group (RMAG) and the Northern Ireland Regional Audit Advisory Committee (NIRACC) to become GAIN (Guidelines and Audit Implementation Network). The work in promoting clinical excellence will continue through this new process.

CREST wishes to thank the members of the sub group and all who have contributed in any way to the development of these guidelines.

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<http://www.dhsspsni.gov.uk/index/hss/gain.htm>

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CONTENTS

Page No

Section 1.	What is neuropathic pain?	4
Section 2.	How do I diagnose neuropathic pain?	5
	2.1 Diagnostic Criteria	
	2.2 Clinical Evaluation	
Section 3.	What are the initial treatment options for neuropathic pain?	7
	3.1 Non-pharmacological Interventions	
	3.2 Pharmacological Interventions	
	3.3 Review Appointment	
Section 4.	Urgent referral to the specialist pain clinic	11
Section 5.	What treatment options are available in specialist pain clinics?	12
	5.1 Specialist Pharmacological Interventions	
	5.2 Interventional Therapies	
	5.3 Pain Management Programmes	
Section 6.	Where can I get more information on resources?	16
Section 7.	References	17
Section 8.	Members of CREST subgroup for Neuropathic Pain	21
Section 9	Appendix 1: Diagnostic tools for neuropathic pain	24



FOREWORD

Neuropathic pain arising as a result of a lesion or disease of the somatosensory system affects 1.5% of the population and remains difficult to diagnose and treat. These guidelines are produced to assist those who see sufferers infrequently and who wish to initiate therapy or refer on appropriately.

A multiprofessional group all of whom work in the field of pain management has produced this guidance, with the help of a patient representative. I wish to acknowledge their enthusiasm and professionalism in developing these guidelines. Their names are listed in section 8. I would also like to thank the much wider group of health care professionals who attended the initial workshop, advised on early drafts, checked references or otherwise assisted the main group in its deliberations.

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1. What is neuropathic pain?

Neuropathic pain is a very common problem in many neurological diseases and is estimated to affect up to 1.5% of the population. The International Association for the Study of Pain (IASP) 1994 definition of neuropathic pain has been updated by the Neuropathic Pain Working Group 2006 as ‘Pain arising as a direct consequence of a lesion or disease affecting the somatosensory system’.

Neuropathic pain may be classified by:

- underlying disease (e.g. diabetic neuropathy, multiple sclerosis)
- site of lesion (e.g. peripheral nerve lesion, spinal cord)
- underlying mechanism

Common conditions associated with neuropathic pain:

Diabetic neuropathy	Post incision chronic pain
Central post stroke pain	Brachial plexus avulsion
Spinal cord injury pain	Trigeminal neuralgia
Multiple sclerosis	HIV associated neuropathy
Polyneuropathy	Neuropathy secondary to vascular insufficiency
Complex regional pain syndrome	Spinal surgery
Phantom limb pain	Amputation
Alcoholism	Cancer chemotherapy
Post-herpetic neuralgia	
Back, leg and hip problems (sciatica or nerve root pain)	

Significant and persistent chronic pain is a common reason for primary care consultations. Physical, social and psychological factors should be assessed from an early stage and management strategies should be offered where appropriate.

2.0 How do I diagnose neuropathic pain?

2.1 Diagnostic Criteria

The diagnosis of neuropathic pain relies on accurate history and examination. Diagnostic tools such as the DN4 or LANSS scoring tools may be useful. The S-LANSS is designed for self-completion by patients. All of these tools reliably predict the presence of neuropathic pain (Appendix 1 refers).

Characteristics of neuropathic pain can be defined within the following criteria:

Spontaneous (Stimulus independent):

- Constant burning sensation
- Intermittent shooting
- Lancing sensations
- Electric shock-like pain
- Dysaesthesias (abnormal and unpleasant sensations)
- Paraesthesias (abnormal, but not unpleasant sensations)

Stimulus evoked pains (Elicited by mechanical, thermal or chemical stimulus):

- Hyperalgesia (increased response to normally painful stimulus)
- Mechanical allodynia (pain from non-painful stimuli)
- Dynamic - brush evoked
- Static - pressure evoked
- Cold allodynia (pain evoked by cold stimulus)

2.2 Clinical Evaluation

An assessment of chronic pain should be multidimensional as patients with chronic pain often present with complex problems that require multidisciplinary management. To differentiate between nociceptive, neuropathic, psychogenic and mixed pain it is necessary to consider the following factors:-

- Use of diagnostic tools to differentiate pain (Appendix 1)

- Causes of neuropathic pain (see common conditions associated with neuropathic pain listed previously)
- History and onset of symptoms
- Location, quality, intensity and duration of pain
- Functional impact including daily activities and sleep pattern
- Psychological factors including effect on mood
- Response to previous treatments

3.0 What are the initial treatment options for neuropathic pain?

Treatments should include both non-pharmacological and pharmacological interventions. Education on the nature of the condition and realistic expectations regarding treatment options must be given at an early stage, for example clients may be advised that current treatment may not be curative but self-management may be an achievable and worthwhile goal.

3.1 Non-pharmacological interventions

Non-pharmacological treatments have the lowest risks of adverse side effects and must be offered early.

For clients with minimal psychosocial difficulties advice should be offered on:

- Maintaining activity levels
- Remaining at work
- Avoiding bed rest

This may include referral to:

- **Physiotherapy:** mobilisation, exercise, TENS and Acupuncture
Evidence supporting the use of TENS and Acupuncture is limited, however given their presumed safety these treatments should be offered whenever appropriate
- **Occupational Therapy:** management of physical, social and psychological functional difficulties in areas of personal care, work and leisure
- **Clients with predominantly psychological difficulties:** referral onward to Psychology may be required
- **Clients with significant physical, social and psychological functional difficulties:** referral onward to pain management programme may be appropriate for individual or group support in helping to develop a range of coping strategies

3.2 Pharmacological Interventions

- Neuropathic pain can be treated by unconventional analgesics e.g. antidepressants, anticonvulsants as well as conventional medications e.g. opioids

- Some unconventional analgesics e.g. tricyclic antidepressants, are used outside their normal licensed indications at doses which may be lower than those for their primary indication
- The starting dose and any titration of each pharmacological intervention should be planned, taking into consideration the potential side-effects and interactions with other medication that the patient may be taking
- For full prescribing information of pharmacological agents, see the most recent copy of the British National Formulary (BNF) or consult the Summary of Product specification (SPC)

See Table 1 for 1st line agents recommended for neuropathic pain.

Drug Name	Dose and Route	Maximum Daily Dose	Dose Titration & Duration of Trial	Side-effects/Comments
Tricyclic antidepressants				
Amitriptyline	Initially 10 to 25mg daily at night (oral).	Up to 75mg daily (higher doses under specialist supervision)	Increase dose by 10 to 25mg weekly. Duration of adequate trial 6-8 weeks at maximum tolerated dosage.	Side-effects: Dry mouth, sedation, cardiotoxicity, postural hypotension, bladder problems, constipation. Give dose at night to minimise sedation. Unlicensed for neuropathic pain. Use in place of amitriptyline if sedation with amitriptyline is problematic. Unlicensed for neuropathic pain.
Nortriptyline	10-50mg daily at night (oral).	Up to 75mg at night (higher doses under specialist supervision)	Increase by 10 to 25mg weekly.	
Anti-epileptics				
Gabapentin	300mg orally on day 1, 300mg twice daily on day 2, 300mg three times daily on day 3, increased according to response in steps of 300mg daily.	3.6g	Increase dose by 300mg every day to a max of 3.6g total daily dose. Duration of adequate trial 3-8 weeks for titration plus 1-2 weeks at maximum tolerated dosage.	Side-effects: Dry mouth, dizziness and cognitive impairment. Licensed for treatment peripheral neuropathic pain (age >18 years).
Pregabalin	150mg daily in 2-3 divided doses (oral), increased if necessary.	600mg	Increase after 3-7 days to 300mg daily in 2-3 divided doses, increased if necessary after 7 days to max 600mg daily in 2-3 divided doses.	Licensed for treatment peripheral and central neuropathic pain (age > 18years). Consider particularly if dosage schedule more suitable for patient or if side-effects develop with gabapentin.
Carbamazepine (Trigeminal neuralgia only)	Initially 100mg 1-2 times daily (oral) increased gradually according to response. Usual dose 200mg 3-4 times daily.	1.6g	Small doses should be used initially to minimise side-effects e.g. dizziness. Build up dose slowly with increments of 100-200mg every 2 weeks.	Licensed for treatment of paroxysmal pain of trigeminal neuralgia. Counsel patient to recognise signs of blood, hepatic or skin disorders.

Duration of trial:

If partial response occurs to 1st line drug, consider adding in another 1st line drug from the other class and consider topical agent.

Additional Therapies:

Topical agents:

Lidocaine 5% medicated plaster for topical application to the affected area is licensed for the treatment of pain caused by post-herpetic neuralgia. Some pain relief may occur on the 1st day of using the plaster. It may take up to 2-4 weeks until the full pain-relief effect is evident. Consult product literature for full prescribing information.

Strong opioids:

Strong opioids may be an effective agent when other therapies fail. The dose should be titrated and response to the drug regularly reviewed.

Simple analgesics:

Paracetamol, weak opioids (tramadol, codeine) and Non-Steroidal Anti-Inflammatory Drugs (NSAIDs/Cox II inhibitors) may be useful adjuvant therapies.

See also section 5 for specialist pharmacological interventions

3.3. Review Appointment

Ongoing follow up will allow the healthcare team to assess any improvements and will inform decisions to change or continue with current treatments. Quality of life improvement and functional mood and sleep assessments are important factors to consider alongside an objective pain assessment.

Decisions should be made to adjust therapy if needed. The patient should be engaged in this process with ongoing education and advice provided. Patients who are failing to respond to therapy will need referral onwards for further specialist management of their physical, social and psychological functional difficulties.

4. Urgent referral to the specialist pain clinic

- Complex Regional Pain Syndrome (CRPS) warrants an urgent referral as early interventions can prevent long-term disability
- There are two types of CRPS – type 1 and type 2:

CRPS Type 1 (Previously known as reflex sympathetic dystrophy (RSD))

Clinical features:

- Presence of an initiating noxious event or a cause of immobilisation
- Continuing pain with neuropathic features (e.g. allodynia or hyperalgesia)
- Evidence of oedema from time to time, change in skin blood flow, abnormal sudomotor activity in the region of pain
- Exclusion of other medical conditions that would otherwise account for the degree of pain and dysfunction

CRPS Type 2 (Previously known as causalgia)

Clinical features:

- All the above features along with the clinical signs and history consistent with a nerve injury

This is a group of patients who need a prompt diagnosis and an urgent referral to improve their long-term morbidity. It has been shown that early initiation of appropriate treatment can reverse the signs and symptoms.

5.0 What treatment options are available in specialist pain clinics?

5.1 Specialist Pharmacological Interventions

- **Capsaicin:** licensed for neuropathic pain but the intense burning sensation during initial treatment may limit use. Capsaicin applied topically may improve symptoms of post-herpetic neuralgia, nerve injury and mixed neuropathic pain conditions
- **Second-line anticonvulsant drugs** (unlicensed for neuropathic pain) e.g. lamotrigine, sodium valproate, clonazepam are efficacious but have significant side effects. If used in combination, specialist supervision is advised
- **Ketamine:** unlicensed for neuropathic pain. It may be administered orally or by intravenous infusion. Side effects, including psychomimetic effects, limit its usefulness
- **Canabinoids:** Nabilone (unlicensed) and Sativex (licensed in Canada) act on central and peripheral cannabinoid receptors
- **Strong opioids:** Morphine, oxycodone and transdermal fentanyl and buprenorphine all exhibit efficacy in neuropathic pain. There is no robust evidence that one is more effective than the others
- **Lidocaine** by intravenous infusion may be effective. Patients who respond may derive benefit from oral mexiletine
- **Selective serotonin re-uptake inhibitors and duloxetine** (licensed for painful diabetic neuropathy) which inhibit both the re-uptake of serotonin and noradrenaline, are effective

Most of these agents have significant side-effects which may limit their use.

5.2 Interventional Therapies

- Interventional treatments for the management of neuropathic pain are well described and available at Pain Clinics throughout Northern Ireland
- Interventional treatments for neuropathic pain should be offered to any patient whose pain is not adequately treated with first and second line drugs or for patients with side-effects from medication
- Invasive treatments should usually be carried out as part of a multidisciplinary treatment plan
- Patients for spinal cord stimulation or implantable devices may benefit from pre-treatment psychological evaluation
- As with medication, success from interventional therapies may be diminished by concordant psychosocial issues especially depression and anxiety

5.2 (i) Steroid injection:

Injection of steroid can be targeted at a peripheral site:

- A common procedure is to inject steroid onto the suspected site of nerve injury, (scar neuroma or peripheral nerve injury) following trauma or surgery. The steroid is commonly mixed with local anaesthetic. Benefits are generally for several months before repeat procedure or alternative therapy is needed. Steroid side-effects are minimised by limiting the dose (typically 20-40mg methylprednisolone or equivalent) and number of injections each year (typically 2-4)
- Steroids may also be injected more centrally onto the dorsal root ganglion or into the epidural space:
 - * **Dorsal root ganglion injection** is indicated for nerve root pain, most commonly associated with a lumbar intervertebral disc prolapse or failed back surgery syndrome. The injection is completed under x-ray control. Evidence to support this treatment is mixed and response to injection is unpredictable
 - * **Injection of steroids into the epidural space**
The injection is technically straightforward in most patients and relatively safe. Patients must discontinue anticoagulants beforehand as bleeding into the epidural space can result in spinal cord injury. Complete pain relief following epidural is unlikely and results are unpredictable. The duration of any benefit is usually limited to a number of months

5.2 (ii) Neuromodulation:

A range of therapies which aim to alter the perception of pain by stimulation or inhibition of neural pathways:

Spinal cord stimulation (SCS):

A recognised treatment for the management of resistant neuropathic pain. Treatment involves inserting one or two epidural electrodes which are then connected to a power source similar to a pacemaker power source. There are a number of neuropathic pains which can be considered for such treatment, including:

- Complex Regional Pain Syndrome (CRPS), type 1 (previously known as Reflex Sympathetic Dystrophy)
- Resistant radicular pain
- Failed Back Surgery Syndrome: Persistent leg or back pain following back surgery
- Peripheral nerve injury e.g. following amputation or limb injury
- Other neuropathic pains generally do not respond as well, although a trial of SCS may be considered if all other treatments fail

Pulsed radiofrequency:

An insulated needle is introduced to the site of nerve injury or the dorsal root ganglion. The heat generated creates a temporary lesion of the nerve tissue. Duration of benefit is often several months. Indications include peripheral nerve injury and radicular pain.

5.2 (iii) Blockade of the sympathetic nervous system:

This may provide relief in patients whose neuropathic pain is maintained via this system (Sympathetic-maintained pain). The sympathetic chain can be treated in the cervical, thoracic and lumbar regions with local anaesthetic, thermal radiofrequency or nerve destruction using chemical destruction. Duration of effect depends on method of treatment.

5.3 Pain Management Programmes

Although most people attending pain management programmes have musculoskeletal pain, the methods are applicable in the management of neuropathic pain.

The Pain Management Programme aims to improve the physical, psychological and social dimensions of quality of life for people with persistent pain, using a multidisciplinary team, working according to behavioural and cognitive principles. Pain relief is not a primary goal although improvements in pain have been reported. Return to work or improved function at work is an important goal for many, but not for all.

The programme is usually delivered in a group format to normalise pain experience, maximise possibilities of learning from other group members and for economy and consists of education and guided practice in the following areas:-

- anatomy, physiology and psychology of pain
- physical reconditioning
- gradual restoration of function in purposeful activity including self-care, work and leisure
- relaxation/stress management
- self management of flare-ups and set-backs
- use of cognitive strategies to deal with the psychological effects of persistent pain and stress
- use of medication

Exclusion criteria for these programmes commonly include; limited life expectancy or rapidly progressing disease, psychosis and severe cognitive impairment.

Pain management programmes significantly reduce distress and disability, significantly enhance coping and improve various measures of physical performance. Where vocational training has been included in the package, return to work is also significantly enhanced.

There is also evidence for decreased use of healthcare resources in terms of numbers of consultations and reduction of medication.

6. Where can I get more information on resources?

Useful websites:

The British Pain Society www.britishpainsociety.org

International Association for Study of Pain www.iasp-pain.org

Pain Talk www.pain-talk.co.uk

Pain Web www.thepainweb.com

CREST NI www.crestni.org.uk/guidelines

Neuropathy Trust www.neurocentre.com

Guidelines and Audit Implementation Network (GAIN)

<http://www.dhsspsni.gov.uk/index/hss/gain.htm>

Specialist Pain Clinics in Northern Ireland:

- Altnagelvin Area Hospital
- Antrim Area Hospital
- Belfast City Hospital
- Causeway Hospital, Coleraine
- Craigavon Area Hospital
- Daisy Hill Hospital, Newry
- Erne Hospital, Enniskillen
- Mater Hospital, Belfast
- Musgrave Park Hospital, Belfast
- Tyrone County Hospital, Omagh
- Ulster Hospital, Dundonald

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9. Appendix 1: Diagnostic tools for neuropathic pain.

(i) S-LANSS diagnostic tool (Bennett et al 2005)

(self-completed by patient)

- On the scale below, please indicate how bad your pain (that you have shown on the above diagram) has been in the last week where: '0' means no pain and '10' means pain as severe as it could be.

NONE 0 1 2 3 4 5 6 7 8 9 10 SEVERE PAIN

- Below are 7 questions about your pain (the one in the diagram).
- Think about how your pain that you showed in the diagram has felt **over the last week**. Put a tick against the descriptions that best match your pain. These descriptions may, or may not, match your pain no matter how severe it feels.
- Only circle responses that describe your pain.

1. In the area where you have pain, do you also have 'pins and needles', tingling or prickling sensations?

- (a) NO – I don't get these sensations (0)
- (b) YES – I get these sensations often (5)

2. Does the painful area change colour (perhaps looks mottled or more red when the pain is particular bad?)

- (a) NO – The pain does not affect the colour of my skin (0)
- (b) YES – I have noticed that the pain does make my skin look different from normal (5)

3. Does your pain make the affected skin abnormally sensitive to touch? Getting unpleasant sensations or pain when lightly stroking the skin might describe this.

- (a) NO – The pain does not make my skin in that area abnormally sensitive to touch. (0)
- (b) YES – My skin in that area is particularly sensitive to touch (3)

4. **Does your pain come on suddenly and in bursts for no apparent reason when you are completely still? Words like ‘electric shocks’, jumping and bursting might describe this.**
- (a) NO – My pain doesn’t really feel like this (0)
- (b) YES – I get these sensations often (2)
5. **In the area where you have pain, does your skin feel unusually hot like a burning pain?**
- (a) NO – I don’t have burning pain (0)
- (b) YES – I get burning pain often (1)
6. **Gently rub the painful area with your index finger and then rub a non-painful area (for example, an area of skin further away or on the opposite side from the painful area). How does this rubbing feel in the painful area?**
- (a) The painful area feels no different from the non-painful area (0)
- (b) I feel discomfort, like pins and needles, tingling or burning in the painful area that is different from the non-painful area (5)
7. **Gently press on the painful area with your finger tip then gently press in the same way onto a non-painful area (the same non-painful area that you chose in the last question). How does this feel in the painful area?**
- (a) The painful area does not feel different from the non-painful area (0)
- (b) I feel numbness or tenderness in the painful area that is different from the non-painful area (3)

Scoring: a score of 12 or more suggests pain of a predominantly neuropathic origin.

SCORE _____

(ii) **LANSS diagnostic tool (Bennett, M. 2001)**

(administered by Healthcare Professional)

THE LANSS PAIN SCALE

Leeds Assessment of Neuropathic Symptoms and Signs

NAME _____ DATE _____

This pain scale can help to determine whether the nerves that are carrying your pain signals are working normally or not. It is important to find this out in case different treatments are needed to control your pain.

A. PAIN QUESTIONNAIRE

- Think about how your pain has felt over the last week.
- Please say whether any of the descriptions match your pain exactly.

1. **Does your pain feel like strange, unpleasant sensations in your skin? Words like prickling, tingling, pins and needles might describe these sensations.**
 - (a) NO – My pain doesn't really feel like this (0)
 - (b) YES – I get these sensations quite a lot (5)

2. **Does your pain make the skin in the painful area look different from normal? Words like mottled or looking more red or pink might describe the appearance.**
 - (a) NO – My pain doesn't affect the colour of my skin (0)
 - (b) YES – I've noticed that the pain does make my skin look different from normal (5)

3. **Does your pain make the affected skin abnormally sensitive to touch? Getting unpleasant sensations when lightly stroking the skin, or getting pain when wearing tight clothes might describe the abnormal sensitivity.**
 - (a) NO – My pain doesn't make my skin abnormally sensitive in that area (0)
 - (b) YES – My skin seems abnormally sensitive to touch in that area (3)

4. **Does your pain come on suddenly and in bursts for no apparent reason when you're still? Words like electric shocks, jumping and bursting describe these sensations.**
 - (a) NO – My pain doesn't really feel like this (0)
 - (b) YES – I get these sensations quite a lot (2)

5. Does your pain feel as if the skin temperature in the painful area has changed abnormally? Words like hot and burning describe these sensations

- (a) NO – I don't really get these sensations (0)
- (b) YES – I get these sensations quite a lot (1)

B. SENSORY TESTING

Skin sensitivity can be examined by comparing the painful area with a contralateral or adjacent non-painful area for the presence of allodynia and an altered pin-prick threshold (PPT).

1. ALLODYNIA

Examine the response to lightly stroking cotton wool across the non-painful area and then the painful area. If normal sensations are experienced in the non-painful site, but pain or unpleasant sensations (tingling, nausea) are experienced in the painful area when stroking, allodynia is present.

- (a) NO, normal sensation in both areas (0)
- (b) YES, allodynia in painful area only (5)

2. ALTERED PIN-PRICK THRESHOLD

Determine the pin-prick threshold by comparing the response to a 23 gauge (blue) needle mounted inside a 2 ml syringe barrel placed gently on to the skin in a non-painful and then painful areas.

If a sharp pin prick is felt in the non-painful area, but a different sensation is experienced in the painful area e.g. none/blunt only (raised PPT) or a very painful sensation (lowered PPT), an altered PPT is present.

If a pin-prick is not felt in either area, mount the syringe onto the needle to increase the weight and repeat.

- (a) NO, equal sensation in both sides (0)
- (b) YES, altered PPT in painful area (3)

SCORING

Add values in parentheses for sensory description and examination findings to obtain overall score.

TOTAL SCORE (maximum 24)

If score < 12, neuropathic mechanisms are **unlikely** to be contribution to the patient's pain.

If score ≥ 12, neuropathic mechanisms are **likely** to be contributing to the patient's pain

(iii) DN4 diagnostic tool (Bouhassira et al 2005)

If answer yes to 4 or more items, neuropathic mechanisms are likely to be contributing to pain.

DN4 Questionnaire

Please complete this questionnaire by ticking one answer for each item in the 4 questions below:

INTERVIEW OF THE PATIENT

Question 1: Does the pain have one or more of the following characteristics?

- 1 - **Burning**
- 2 - **Painful cold**
- 3 - **Electric Shocks**

yes	no
<input type="checkbox"/>	<input type="checkbox"/>
<input type="checkbox"/>	<input type="checkbox"/>
<input type="checkbox"/>	<input type="checkbox"/>

Question 2: Is the pain associated with one or more of the following symptoms in the same area?

- 4 - **Tingling**
- 5 - **Pins and Needles**
- 6 - **Numbness**
- 7 - **Itching**

yes	no
<input type="checkbox"/>	<input type="checkbox"/>
<input type="checkbox"/>	<input type="checkbox"/>
<input type="checkbox"/>	<input type="checkbox"/>
<input type="checkbox"/>	<input type="checkbox"/>

EXAMINATION OF THE PATIENT

Question 3: Is the pain located in an area where the physical examination may reveal one or more of the following characteristics?

- 8 - **Hypoesthesia to touch**
- 9 - **Hypoesthesia to prick**

yes	no
<input type="checkbox"/>	<input type="checkbox"/>
<input type="checkbox"/>	<input type="checkbox"/>

Question 4: In the painful area, can the pain be caused or increased by:

- 10 - **Brushing**

yes	no
<input type="checkbox"/>	<input type="checkbox"/>

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