York and Scarborough Teaching Hospitals NHS Foundation Trust

Guidelines for use of Clonazepam for pain control in Palliative Care patients

The International Association for the Study of Pain (IASP 2011) defines neuropathic pain as 'pain by a lesion or disease of the somatosensory nervous system'. Examples of common conditions that have peripheral neuropathic pain as a symptom are painful diabetic neuropathy, post-herpetic neuralgia, trigeminal neuralgia, 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. 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, itching and a sensation of pins and needles. People may also describe symptoms of allodynia (pain caused by a stimulus that does not normally provoke pain), hyperalgesia (an increased response to a stimulus that is normally painful), anaesthesia dolorosa (pain felt in an anaesthetic [numb] area or region), and sensory gain or loss (IASP 2011).

If Clonazepam is being considered for use in neuropathic pain the following guidelines should be adhered to:

a) **Consultation with a Palliative Medicine Consultant** is required before starting Clonazepam in all care settings
b) Follow NICE guidance for neuropathic pain before considering Clonazepam https://www.nice.org.uk/guidance/cg173
c) Clonazepam should only be used if NICE approved drugs are ineffective
d) If patients are unable to swallow and on neuropathic pain agents, Clonazepam may be considered as a replacement analgesic
e) Clonazepam may be used in an injectable form (unlicensed in UK) whereas other neuropathic agents cannot
f) As part of the **consent process** for commencing Clonazepam, the patient should be made aware that it is an unlicensed drug and be given **an unlicensed drug information leaflet**
g) Prior to the use of Clonazepam (oral or injectable) complete a Leeds Assessment of Neuropathic Symptoms and Signs **(LANSS** if staff complete, **or S-LANSS** if patient self completes**)** See Appendix 1
h) Complete a **Clonazepam audit tool** as used for audit purposes. See Appendix 2.
   Email or telephone appropriate Hospital Palliative Care Team secretary in either York susan.blanchard@york.nhs.uk 01904 725835 or Scarborough Sue.Salt@york.nhs.uk 01723 342446
i) **Monitor efficacy** - Pain score pre and post administration of Clonazepam
j) **Monitor side effects**

In community setting

k) Clonazepam injection is difficult to procure and requires a consultant written prescription from the hospital pharmacy to obtain as it is an unlicensed preparation in the UK
l) Clonazepam is generally prescribed for use in a syringe driver only
m) Clonazepam is rarely prescribed as a prn in the community due community healthcare professionals being unfamiliar with the drug
n) All medication changes should be documented on Systm1 and task sent to inform GP

Prescribing information

Dose conversion oral to subcutaneous	Oral Clonazepam has bioavailability of >80% so a 1:1 conversion can be used *but note comments below under compatibility and PVC tubing*
Starting dose in neuropathic pain	Usually 500 microgram in 24 hours
Usual dose range	500 microgram to 4 mg in 24 hours
Formulation	**Unlicensed drug:** import from abroad (used to be licensed in the UK) **Unlicensed route:** licensed iv and im **but can** be used sc **Strength:** Injection 1mg/ml ampoule of solution (1mL) If it is dispensed in the original manufacturers pack it will also come with a diluent (1mL water for injection) for further dilution when given as a bolus The diluent is not required when the injection will be diluted further in a syringe driver
Supply	Clonazepam injection is not readily available in community and is usually dispensed by the Trust hospital pharmacy at York or Scarborough on receipt of a prescription written by a Trust Consultant in Palliative Medicine. We do not hold a large quantity of stock so please liaise closely with pharmacy around repeat supplies
Compatibility data	**PVC tubing:** In theory non PVC tubing should be used as Clonazepam can adsorb to the plastic, but this is not always practical. Take care therefore if switching between pvc and non pvc lines – dose adjustments may be needed **Compatibility with other drugs in syringe driver:** It is generally compatible with commonly used drugs but at some concentrations may not be compatible with cyclizine or dexamethasone **Diluent:** Compatible with water for injection or sodium chloride 0.9%. Sodium chloride may be preferred if administering alone. Water for injection should be used if cyclizine is present but this combination can sometimes be incompatible For more information see • compatibility charts in PFC 7 • syringe driver compatibility on https://book.pallcare.info/ • The Syringe Driver 4th ed (Dickman)
Drug interactions	Clonazepam is metabolised by the hepatic enzyme system cytochrome p450 (CYP3A4), so consider this if patients are on other medication which affects this enzyme. See Scottish Palliative Care Guidelines for further information

References

1. Palliative Care Formulary 7th edition
2. The Syringe Driver 4th edition Andrew Dickman and Jennifer Schneider
3. NICE guidelines https://www.nice.org.uk/guidance/cg173
4. Scottish Palliative Care Guidelines https://www.palliativecareguidelines.scot.nhs.uk/guidelines/medicine-information-sheets/clonazepam.aspx

APPENDIX

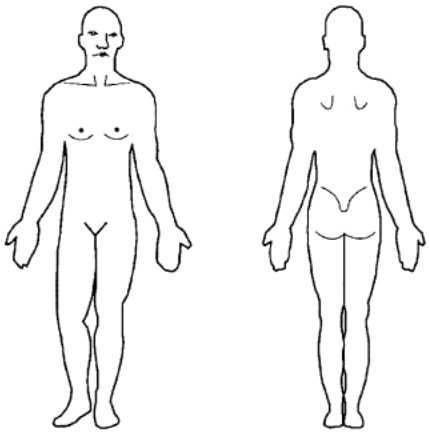
THE S-LANSS PAIN SCORE

Leeds Assessment of Neuropathic Symptoms and Signs (self-complete)

NAME_____ **DATE**_____

- This questionnaire can tell us about the type of pain that you may be experiencing. This can help in deciding how best to treat it.

- Please draw on the diagram below where you feel your pain. If you have pain in more than one area, **only shade in the one main area where your worst pain is.**



- 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**

- On the other side of the page 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.** Please circle the descriptions that best match your pain. These descriptions may, or may not, match your pain no matter how severe it feels.

- Only circle the responses that describe your pain. **Please turn over**.

S-LANSS

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 particularly 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 <u>rub</u> 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 <u>press</u> 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 predominantly neuropathic origin

Appendix 2

Clonazepam audit proforma

Audit number

Setting (inpatient/outpatient)	
Location York/Scarborough	
Indication	a)Pain b)Fitting
Trial of amitriptyline first ? (Yes/No)	
Trial of gabapentin first ? (Yes/No)	
Trial of pregabalin first ? (Yes/No)	
Has NICE guidance been followed? e.g. 2nd line using both TCAD +anticonvulsant together before trying clonazepam? (Yes/No) Which drug combinations and final doses	
If above not started, was there a documented reason why NICE guidance not followed? E.g. a) Pt unable to swallow & no feeding tube b) Pt in last days of life and previously been on adjuvants for neuropathic pain. c) Pt vomiting d) Unable to take TCAD as CI(arrhythmias) e) Unable to take anticonvulsant as CI(renal impairment)	Reason for not following NICE guidance
Initial dose of clonazepam	
Dose clonazepam titrated up to	
SC or oral	
Any documented benefit?	
Was a pain score documented **before** use of clonazepam? If yes state pain score	
Was a pain score documented **after** use? If yes state pain score	
Was the LANSS/S-LANSS assessment of neuropathic pain used before clonazepam use? Yes /No	If Yes LANSS/SLANSS score
Any documented side effects?	
Any medication changes made at same time to account for a)side effects or b)pain improvement? If Yes which medication	
Who was it started by (Consultant/Registrar/Specialist nurse)	
If not started by a Consultant is there documentation of discussion with a consultant?	
Was a leaflet for unlicensed medication given to the patient? Yes/No	

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Return to York Hospital Palliative Care Team or scan and email to the secretary.