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Barnsley Pregabalin Prescribing Guidelines for Neuropathic Pain

Pregabalin (Lyrica®) was launched in the UK in 2004 for the management of epilepsy, then subsequently licensed for the treatment of neuropathic pain, and generalised anxiety disorder (GAD). This guidance focuses on the prescribing of pregabalin in neuropathic pain for which pregabalin has a green traffic light status. Pregabalin has an amber classification when used for the treatment of epilepsy and an amber-G classification when used for GAD.

Summary of key prescribing points:

- Consider the potential for misuse before prescribing pregabalin. There are published reports of both pregabalin and gabapentin abuse, particularly in the substance misuse population. Also consider the potential for illicit diversion either by choice or through coercion.
- Pregabalin has been associated with a rare risk of severe respiratory depression, even in patients not receiving concomitant opioid medicines. Dose adjustments may be necessary in patients at higher risk.[1]
- Pregabalin use in the first trimester of pregnancy has been shown to be associated with a slightly increased risk of major congenital malformations. Patients should use effective contraception and avoid pregabalin in pregnancy unless clearly necessary.[2]
- Ensure all prescriptions for pregabalin are **reviewed on a regular basis** by limiting the authorisation period.
- Ensure prescriptions are **not ordered more frequently** than necessary, without valid reason.
- Exercise vigilance for all requests for pregabalin by name.
- **Always** confirm new requests with previous prescriber for new patients / temporary residents etc.
- If a gabapentinoid is necessary, consider changing over to gabapentin.
- **Regularly review and assess the patient** with a view to dose reduction.
- Ensure the dose is optimised to **TWICE a day** (BD) dosing, rather than THREE times a day (TDS), as this is more cost effective.[3] It also limits the amount of medication available for illicit diversion. It is more cost effective to prescribe the capsule formulation.
- Pregabalin was reclassified as a Schedule 3 Controlled drug in April 2019. The maximum quantity of Schedule 3 drugs prescribed should not exceed 30 days supply. Consider 7 day's supply where there is concern.
- Discuss any concerns regarding misuse with Humankind Barnsley Recovery Steps.
- If patient participates in a needle exchange scheme, be aware the contents of capsules can be opened and injected. There have been verbal reports that pregabalin may be preferred to heroin.

Background

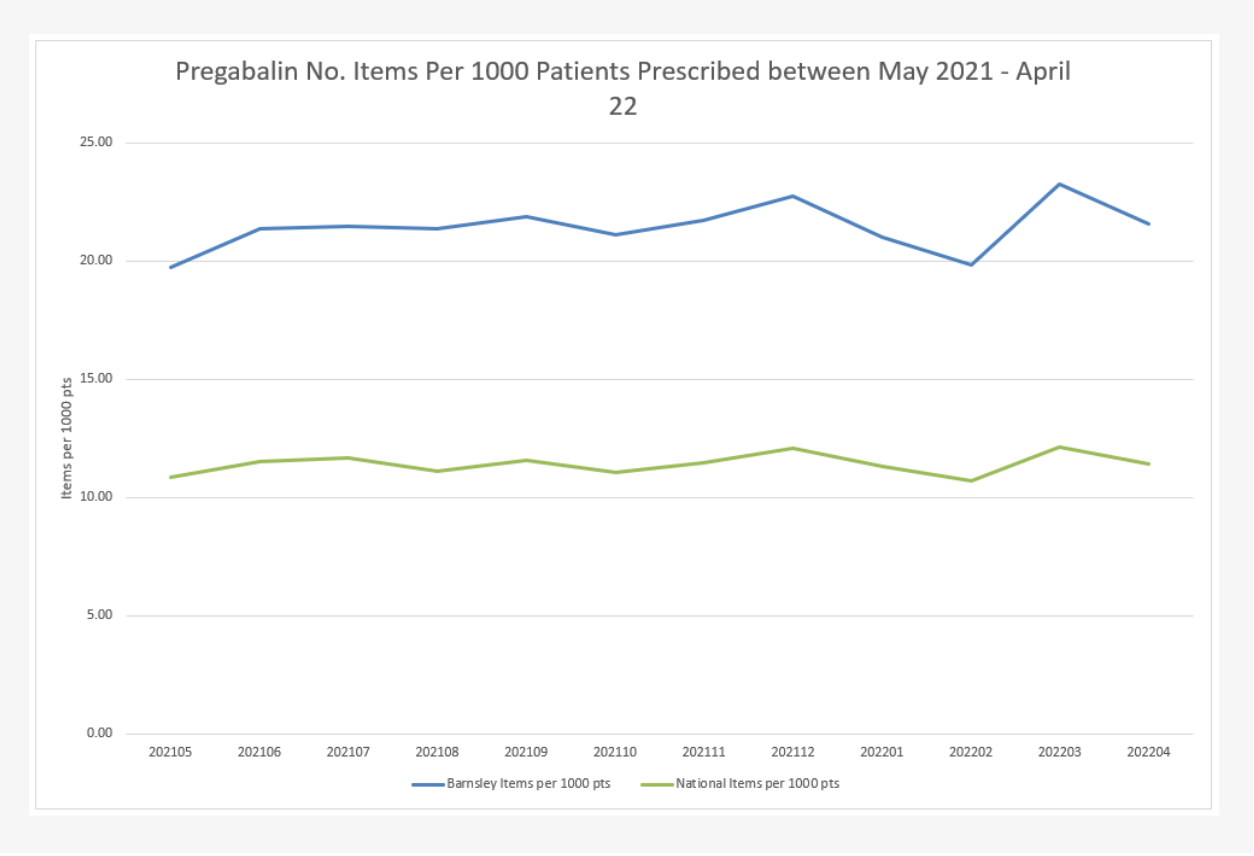
NICE guidance[4] published in November 2013 (CG173) suggests offering a choice of amitriptyline, duloxetine, gabapentin or pregabalin as initial treatment for **ALL** neuropathic pain (except trigeminal neuralgia) in adults in non-specialist settings. If the initial drug is not effective or tolerated, then one of the other 3 drugs should be tried. If the second or third drugs remain ineffective or not tolerated then consideration should be given to switching to the remaining options. Local guidance has been produced to support in implementing the NICE guidance (see Appendix 1).

Pregabalin prescribing in Barnsley

Usage of pregabalin is increasing across the NHS. Prescribing in NHS Barnsley CCG is above the national average and there is a wide variation in the number of prescriptions issued across Barnsley GP Practices.[5]

The frequency of prescribing of pregabalin and gabapentin are significantly higher in Barnsley than in other local CCGs and compared to the England and regional averages.[5] The following chart compares items/1000 patients for pregabalin with the England average across a 12-month period.

ePACT data Barnsley and England Pregabalin Prescribing May2021 – April 2022



Local prescribing reviews have shown that the largest part of this prescribing is for neuropathic pain, initiated both in primary and secondary care. The increased level of pregabalin prescribing seems to suggest that local guidance and NICE guidance is not being followed.

Illicit Use

- In recent years, it has become apparent that pregabalin is also used illicitly. Both pregabalin and gabapentin are highly sought after because of their ability to enhance the effects of opiates and alcohol, and also because of their own inherent abuse potential.
- Pregabalin is reported as having alcohol-like effects mixed with euphoria, thus producing a recreational high. Emerging evidence shows pregabalin to have abuse potential particularly in the substance misuse population.[6]
- A review carried out by the Canadian Agency for Drugs and Technologies in Health (CADTH) concluded that whilst pregabalin was not likely to be abused by non-drug abusing subjects, it does have euphorigenic activity and this may be subject to abuse in susceptible populations and may be associated with an abuse liability.[7]
- Drug treatment services are regularly reporting misuse of gabapentinoids, both prescribed and illicitly sourced. GPs are reporting increasing pressure from patients to prescribe it as an analgesic for chronic pain.
- Pregabalin and gabapentin abuse has been identified as being prevalent in the local prison population.[6]

Prescribing Advice for Neuropathic Pain

Neuropathic pain is very challenging to manage because of the heterogeneity of its aetiologies, symptoms and underlying mechanisms.[8] 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. 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.

At present, there are no recognised guidelines for the assessment of neuropathic pain. Consequently use of an assessment tool may assist the clinician in their assessment and diagnosis.

Organisations may use questionnaires such as PainDETECT or Leeds Assessment of Neuropathic Signs and Symptoms[9] (LANSS) to identify if neuropathic is likely (See Appendix 2 for links).

Once a diagnosis of neuropathic pain has been made, clinicians are encouraged to follow NICE CG173[4] and local prescribing guidelines (See Appendix 1)

Expert based recommendations from the British Pain Society suggest asking a patient to keep a short-term diary of response to a drug and how it is taken because patients often do not adhere to the instructions.[10]

Patients and prescriptions should be regularly reviewed to assess and monitor the effectiveness of the treatment.

Each review should assess the need for continued treatment. Once satisfactory pain control is achieved with any medication, treatment should then be continued. Pharmacological interventions should be increased to their 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 30-50% reduction in pain is reasonable.[10] If the patient has not shown sufficient benefit within eight weeks of reaching the maximum tolerated dose, except when moving to combination therapies, drug treatment should be reduced gradually and stopped.[11]

It is suggested that there should be a reduction in dose on an annual basis to ascertain ongoing effectiveness. [12]

If pregabalin is indicated, prescribers should be mindful that twice daily (BD) dosing is convenient for patients, and more cost effective than three times a day (TDS) dosing, as pregabalin has a flat pricing structure across all available strengths. The total daily dose can be prescribed twice a day without any loss in efficacy. (150mg capsules BD dosing: £2.58 /28 days vs. 100mg TDS: £4.11/28 days). [3]

It is also important to ensure those patients initiated on pregabalin by specialist pain management services, or other condition specific services, are also reviewed regularly and that a pain management plan is in place. Once a patient is discharged from the service, the clinician is advised to request a copy of the patient's final pain assessment so that future progress can be monitored.

In those patients with a history of substance misuse, or for those who have been in prison, be particularly cautious about the prescribing of pregabalin, and gabapentin. Patients may request directly by name stating that other treatments haven't worked. Be aware there is also the potential for non-drug users to sell prescribed drugs on the street. The current street value is at least £1 per tablet. [13]

Doncaster Prison Cluster will confirm discharge medication for previous patients on request. GPs are advised not to prescribe until they have confirmed as such. Local prison GPs very rarely initiate pregabalin due to the discussed issues. Where use of gabapentin or pregabalin cannot be avoided, it is considered preferable to use gabapentin as it is less addictive, less psychoactive and safer in overdose than pregabalin. Doncaster Prison Cluster is also proactive in the assessment of neuropathic pain and reduction of pregabalin and gabapentin in those patients already prescribed such medications.

Practices can contact the relevant healthcare departments on the following numbers:

HMP Doncaster:	Tel 01302 764 343 practiceplusgrp.doncasterhealthcare@nhs.net
HMP Lindholme:	Tel 01302 524701
HMP Moorland:	Tel 01302 523 139
HMP Hatfield: (Formerly known as HMP Moorland Open)	Tel 01405 746 563

It would also be prudent to discuss any prescribing issues with substance misuse services as they also share concerns regarding the increasing misuse of pregabalin in the region.

Please telephone the treatment provider Humankind Barnsley Recovery Steps on (01226) 779066. You can also request to speak with Dr Fleur Ashby, Clinical Director Barnsley Recovery Steps, on the same number for advice around prescribing amongst substance misusers.

This guideline was ratified at the Area Prescribing Committee on 15th June 2022 (due for review June 2025).

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South Yorkshire
Integrated Care Board

Appendix 1

Drug Management of Neuropathic Pain

(Please note: management of pain with a neuropathic element in palliative care may differ from the guidance below).

Neuropathic pain not responding to simple analgesia and with symptoms such as sleep disturbances, depression and interference with normal daily activities can be managed using the suggested algorithm below. All patients should have regular clinical reviews, and have early reviews following medication changes. Once satisfactory pain control is achieved with any medication, treatment should then be continued. If improvement is sustained consideration may be given to reducing the dose gradually over time following consultation with the patient.

NICE Clinical Guideline (CG173)[1] for the pharmacological management of neuropathic pain and the NICE pathway for managing the long term complications of type 2 diabetes[2] advises initial treatment with one of the four options listed below. If initial treatment with oral medication is not effective or not tolerated, offer one of the remaining three oral drugs. Consider switching again if the second or third drugs tried are also not effective or not tolerated. Due to lack of evidence of safety and cost effectiveness NICE advises against prescribing more than one neuropathic pain drug at the same time e.g. **am**itriptyline concurrently with duloxetine, gabapentin or pregabalin. However, the NICE Guideline Development Group noted that combination treatment may be more practical and more effective than switching to a new treatment and may reduce adverse effects of the individual drugs owing to the combination of lower doses.

*(**Please consult relevant SPC for further information when prescribing these drugs**[3])*

Local guidelines for the prescribing of pregabalin are available at:
http://best.barnsleyccg.nhs.uk/clinical-support/medicines/prescribing-guidelines/Pregabalin%20for%20neuropathic%20pain%20prescribing%20guidelines.pdf

All types of Neuropathic pain (other than trigeminal neuralgia)

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STEP 1

Amitriptyline (where no cautions or contraindications). Licensed for neuropathic pain in adults.

- Start 10mg 6-8pm to reduce 'hangover' effect
- Increase gradually by 10mg/week to an effective or maximum tolerated dose
- Aim for at least 25mg nocte (not above 75mg)
  Doses higher than 75mg should only be considered in consultation with a specialist pain service and should be used with caution in the elderly and patients with cardiovascular disease.

Inadequate response after 8 week trial or not tolerated → discontinue gradually over a minimum of 4 weeks to avoid discontinuation symptoms[4]

↓

STEP 2

Gabapentin (capsules are more cost effective[5]**)** Licensed for treatment of peripheral neuropathic pain in adults e.g. diabetic neuropathy, post herpetic neuralgia. Use in other conditions is off-label.

Caution: Gabapentin has been associated with a rare risk of severe respiratory depression, even in patients not receiving concomitant opioid medicines. Dose adjustments may be necessary in patients at higher risk.[6]

- Start: Day 1=300mg, Day 2=300mg BD, Day 3=300mg TDS
- Slower dose titration in 100mg increments may help improve tolerability e.g. elderly, frail, or if experienced adverse effects with higher doses
- Increase gradually in 300mg/day increments every 2-3 days to an effective or maximum tolerated dose
- Aim for at least 600mg TDS (maximum 1.2g TDS)
- Allow 1 week to reach 1.2g/day, 2 weeks for 2.4g/day and 3 weeks for 3.6g/day
- See drug SPC for dose adjustment in renal impairment

Inadequate response after 8 week trial or not tolerated → discontinue gradually over a minimum of 1 week

STEP 3

Consider whether, pain clinic referral or psychological support is appropriate. Consider referral to pain clinic (or other appropriate service e.g. diabetic clinic) at any time if the patient has severe pain, the pain significantly limits the patient's daily activities and participation, or if the patient's underlying health condition has deteriorated.

Duloxetine Licensed for the treatment of diabetic peripheral neuropathic pain. Use for other conditions is off-label.

- Start 60mg OD (maintenance dose), up to maximum 60mg BD (no evidence at higher dose)
- A lower starting dose of 30mg may be appropriate e.g. if tolerability is a problem
- Contraindicated in severe renal impairment (creatinine clearance <30 ml/min)
- Inadequate response after 8 week trial or not tolerated discontinue gradually over a minimum of 1 to 2 weeks

OR

Pregabalin Licensed for the treatment of peripheral and central neuropathic pain in adults. Use for other conditions is off-label.

Caution: Pregabalin has been associated with a rare risk of severe respiratory depression, even in patients not receiving concomitant opioid medicines. Dose adjustments may be necessary in patients at higher risk[7].

- Start 75mg BD (25mg BD may be required when used in elderly patients). Increase if necessary after 3-7 days to 150mg BD, then further 7 days to maximum 300mg BD. Prescribe as BD dose (no benefit in TDS) and AVOID double dosing e.g. 2 BD
- See drug SPC for dose adjustment in renal impairment

If pregabalin is not effective or not tolerated, discontinue treatment gradually over a minimum of 1 week.

NICE advises against the use of gabapentinoids for managing sciatica as there is no overall evidence of benefit and there is evidence of harm.[8]

Post-Herpetic Neuralgia (Associated with previous herpes zoster infection)

Treat initially with standard oral therapies as per steps 1-3, and/or topical capsaicin cream 0.075%.

If standard therapies fail, or lead to intolerable side effects, consider **lidocaine 5% medicated plasters**.

There is limited, low quality evidence to support their use; however, they may be of value when other treatments have failed.[9]

Prescribe as **Ralvo**® as currently the most cost effective brand of lidocaine plasters (£61 for 30 plasters)[10]

The painful area should be covered with a plaster once daily for up to 12 hours within a 24 hour period.
No more than three plasters should be used at the same time. Each plaster must be worn for no longer than 12 hours. The subsequent plaster-free interval must be at least 12 hours.[3]
Prescribe a trial of **2-4 weeks** initially and then review for effectiveness before the medication is continued as a repeat prescription. If there has been little or no response to treatment → discontinue[3]

Treatment should be reassessed at regular intervals (e.g. every 6 months) to decide whether the amount of plasters needed to cover the painful area can be reduced, or if the plaster-free period can be extended.[3] A 'trial without' can also be considered to assess ongoing need for treatment.[11,12]

NHS
South Yorkshire
Integrated Care Board

Lidocaine plasters are included within the NHS England guidance 'Items which should not routinely be prescribed in primary care: Guidance for CCGs'.[13] They should only be prescribed in primary care when used to treat post-herpetic neuralgia and alternative treatments are contraindicated, not tolerated or ineffective.

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This guideline was ratified at the Area Prescribing Committee on 10th November 2021 (due for review November 2024).

Appendix 2:

Pain Screening Tools and Questionnaires

PainDETECT https://www.pfizerpcoa.com/sites/default/files/pdq_us_enreview_only_3_1_1.pdf

Leeds assessment of Neuropathic signs and symptoms (LANSS) https://www.mdapp.co/lanss-scale-for-neuropathic-pain-calculator-218/