NPS MEDICINEWISE

Revisiting pregabalin

Optimising safety in prescribing for neuropathic pain

Practice Review PBS data

March 2021

*For more information about this Practice Review and additional national and RA[a] data, see **nps.org.au/pbs-pregabalin***

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Your PBS data are provided confidentially to you only and are intended for personal reflection on your practice.
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15 March 2021

Dear Dr Sample,

NPS MedicineWise routinely sends Practice Reviews with a focus on quality use of medicines and medical tests to clinicians to support continuing quality improvement. NPS MedicineWise ran a national program on neuropathic pain in 2018. Here we are revisiting prescribing of pregabalin, including its combination with opioids and benzodiazepines, to raise awareness of potential harmful and hazardous use.[1–5] This Practice Review has been developed in collaboration with GPs and a representative from the Faculty of Pain Medicine, ANZCA and sent to around 30,000 prescribers across Australia.

Deaths involving pregabalin are increasing

There are growing concerns worldwide about risk of harms and misuse with gabapentinoids.[1-3,5-6] Pregabalin is now one of the top ten drugs most frequently implicated in overdose deaths in Victoria.[3] Incidence of pregabalin poisoning is increasing partly because of pregabalin misuse and abuse.[7] The pregabalin product information was recently updated to warn of the risk of misuse, abuse and dependence which can lead to overdose and death, especially when used with other central nervous system depressants.[8] A recent study of patients prescribed pregabalin, using MedicineInsight data, showed that 38% were prescribed an opioid, 13% were prescribed a benzodiazepine and 4% were prescribed both an opioid and a benzodiazepine on the same day.[9]

One in every seven patients prescribed pregabalin appears to be at high risk of misuse[1,2]

Patients at increased risk of pregabalin misuse and harm include those with a history of drug-seeking behaviour,[10] mental health[4] or substance use disorder (particularly opioid use disorder),[2,4] patients with multiple pregabalin prescribers, those who are prescribed higher strengths of pregabalin, are younger (< 55 years), male, or unemployed.[2]

Pregabalin is only PBS-subsidised for neuropathic pain refractory to treatment with other medicines

Pregabalin was the 14th most prescribed medicine on the PBS in 2019–20.[11] MedicineInsight data show that fewer than half of the patients prescribed pregabalin between 2012 and 2018 had recorded diagnoses of neuropathic pain,[9] and international studies have shown high rates of pregabalin prescribing without first diagnosing neuropathic pain.[12,13]

Choosing Wisely Australia

Faculty of Pain Medicine, ANZCA through Choosing Wisely recommends:[14] **"Avoid prescribing pregabalin and gabapentin for pain which does not fulfil the criteria for neuropathic pain."**

What other neuropathic pain resources does NPS MedicineWise have to support you?

- Find resources to support diagnosing neuropathic pain, including demonstration videos of sensory tests, as well as a patient action plan, and information on pregabalin misuse, at nps.org.au/professionals/neuropathic-pain.
- Find consumer information at nps.org.au/consumers/nerve-pain-explained.

Time spent reflecting on this Practice Review has been approved for **2 points (CPD Activity)** under the RACGP CPD Program for the 2020–2022 triennium (activity number: 238034). Questions for reflection are provided for you to record your learning. Answer the CPD questions at nps.org.au/pregabalincpd.

Yours sincerely,

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How to use your confidential Practice Review

This Practice Review is intended to support your prescribing of pregabalin by providing an overview of current best practice recommendations alongside dispensing data related to prescriptions written for your patients. Consider your practice profile and your patients' indications for treatment when reflecting on these data. Recommendations are based on recently updated Therapeutic Guidelines.[15]

Abbreviations used in this report: ANZCA (Australian and New Zealand College of Anaesthetists), CBT (cognitive behavioural therapy), CrCl (creatinine clearance), DN4 (Douleur Neuropathique en 4 questions), RA (remoteness area), SNRI (serotonin and noradrenaline reuptake inhibitor), TCA (tricyclic antidepressant).

Do you diagnose neuropathic pain using both comprehensive history and examination before starting a medicine?

Neuropathic pain is defined as pain caused by a lesion or disease affecting the somatosensory system. Lesions may be peripheral or central. Characteristic features are altered sensation (eg, pins and needles, tingling), sensitisation (ie, allodynia, hyperalgesia) and neuralgia.[15] Pregabalin has efficacy in reducing symptoms of some types of neuropathic pain with greatest evidence for treating diabetic neuropathy and post-herpetic neuralgia.[16] Use of pregabalin for non-neuropathic pain conditions, eg, low back pain, is not supported by evidence and increases risk of harm.[17,18]

Points for reflection

- Take a targeted history and perform a physical examination (including sensory testing) to help determine a probable diagnosis before starting a medicine.[19] Consider using a validated screening tool eg, DN4[20] or painDETECT.[15,21]
- Do not use imaging solely to confirm diagnosis – reserve it for cases where findings will change management.[15]
- Do not use pregabalin as a diagnostic tool for neuropathic pain. Approximately eight patients with neuropathic pain need to be treated with pregabalin for one to achieve a 50% reduction in pain not attributable to placebo.[15]

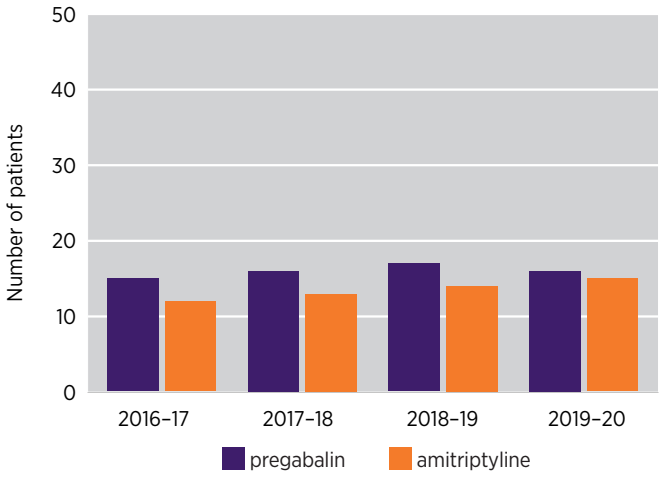
CPD: Question for reflection

- What approach will you take to determine, and record, that a patient's pain has a neuropathic component, before starting pharmacological treatment?

How do you select a medicine for neuropathic pain not adequately managed with non-pharmacological approaches?

In 2019–20 you prescribed pregabalin for 16 patients.

Fig. 1 – Number of patients prescribed pregabalin or amitriptyline by you



Points for reflection

- For chronic neuropathic pain consider a TCA (amitriptyline or nortriptyline) or an SNRI (duloxetine or venlafaxine) or a gabapentinoid (pregabalin or gabapentin). Base choice on individual patient factors and medicine properties.[15]
- Advise patients of common adverse effects,[22] and risk of dependency and misuse with pregabalin.[5,23] Gabapentinoids (particularly pregabalin), TCAs and SNRIs can worsen mood and cause suicidal thoughts. Assess individual patient risk before prescribing.[15]
- For acute neuropathic pain, gabapentinoids may be preferred due to their faster onset of action, but their use may be limited by potential harms. Consider a TCA or SNRI if a gabapentinoid is not appropriate.[15]
- Lidocaine 5% patches are preferred for patients with localised neuropathic pain, particularly for older or frail patients and those on multiple medicines.[15]
- Gabapentin, nortriptyline, duloxetine, venlafaxine and lidocaine are not available on the PBS for neuropathic pain.

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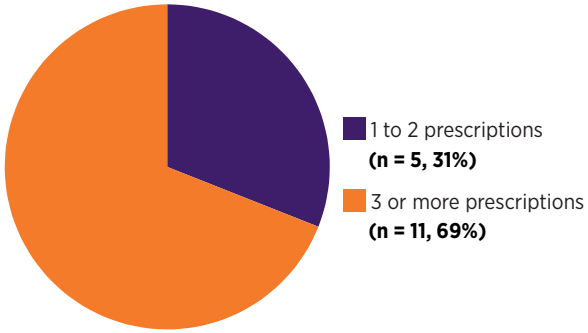
How do you confirm that ongoing treatment with pregabalin is appropriate?

Fig. 2 – Percentage of your patients dispensed a total of 1–2 or 3 or more prescriptions for pregabalin in 2019–20[c]



Points for reflection

- Start with a low dose, increasing slowly, to minimise adverse effects. Benefits should be apparent after around 4 weeks. Continue if effective, and tolerated – if not, consider tapering, then trialling an alternative.[15]
- Trial deprescribing every 3–6 months to assess ongoing benefits and reduce risk of adverse effects.[15]

See back page for further guidance on dosing.

Note: Based on twice-daily dosing, each pack of pregabalin should last 28 days. Due to rounding, percentages may not total 100%.

A 2020 survey by NPS MedicineWise found many consumers felt their early expectations of medicines for nerve pain were not met. Understanding of where to access information and advice, and when and how to stop the medicine, was often poor or very poor.

- Discuss the limited benefits of medicines with the patient and develop a multidimensional plan that includes active strategies for self-management eg, psychological (eg, targeted reassurance, CBT), social and physical activities (eg, walking groups).[15]
- Establish treatment goals for pain relief and function with the patient. Agree upfront when and how a medicine will be stopped.[15]
- Direct patients to trusted sources of information about pain and its management.[15]

CPD: Questions for reflection

- How will you describe treatment options and set expectations with the patient when selecting a medicine?
- How will you assess treatment response and review the ongoing benefit of pregabalin treatment with your patients?

How do you assess for potential misuse when prescribing pregabalin?

In 2019-20, of the **16** patients prescribed pregabalin by you, **31%** also had pregabalin prescribed by another prescriber.

Points for reflection

- Exercise caution when prescribing pregabalin[2] particularly for patients at increased risk of misuse[6] eg, those with multiple prescribers.[2]
- Continue to monitor for signs of tolerance, misuse and/or abuse, such as increase in dose or drug-seeking behaviour.[8,24] The introduction of Real Time Prescription Monitoring (RTPM) may help highlight potential medicine misuse.

How do you minimise risk of potentially dangerous combinations?

Table 1. Patients prescribed pregabalin in 2019-20 by you (16) who were also prescribed opioids and/or benzodiazepines during 2019-20

	By you	Not by you
Also prescribed opioid(s) **or** benzodiazepine(s)[d]	5 (31%)[e]	3 (19%)
Also prescribed both opioid(s) **and** benzodiazepine(s)[d]	2 (13%)[e]	2 (13%)

Note: Medicines may not have been prescribed at the same time.

Points for reflection

- Ask patients what other medicines they are using before you prescribe pregabalin. Explain the significant risks of using pregabalin with medicines such as opioids and benzodiazepines, and with illicit drugs. Tell them to inform any other health professionals they see that they are taking pregabalin.
- Avoid co-prescribing pregabalin with central nervous system depressants if possible.[22] Most fatal overdoses involving pregabalin also involve other drugs, predominantly opioids,[2,4] benzodiazepines,[2,4] alcohol,[2,4] illicit drugs[2] and antidepressants.[4]

CPD: Questions for reflection

- How will you minimise potential risk from interactions and/or pregabalin misuse?
- Considering your prescribing context, how will these data influence your future practice?

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Pregabalin dosing recommendations for acute and chronic neuropathic pain – starting and stopping treatment

Starting treatment	Start with low dose (≤ 75 mg per day) at night. Increase to twice daily after 3–7 days. Increase dose as required based on response and tolerability up to maximum daily dose of 600 mg (300 mg for frail patients and those aged ≥ 70 years). For acute pain, increase at 3–7 day intervals. Increase dose more slowly eg, at 7-day intervals, for chronic pain.[15] Consider uneven dose splitting, with the higher dose in the evening – this can improve sleep and reduce daytime sedation.[22] Pregabalin is usually effective at doses of 300–600 mg per day.[25]
For patients with renal impairment, adjust dose according to CrCl[22]	CrCl 30–60 mL/min: initially ≤ 75 mg per day, maximum daily dose 300 mg CrCl 15–30 mL/min: initially 25 to 50 mg per day, maximum daily dose 150 mg CrCl < 15 mL/min: initially 25 mg per day, maximum daily dose 75 mg
Stopping treatment	Reduce dose gradually over at least a week.[22] Consider tapering slowly to reduce withdrawal symptoms, eg, maximum weekly reductions of 50–100 mg.[26]

Practice profile: provided to help you interpret your prescribing data.

Your Medicare patients and concession card holders

	Medicare card holders	Concession card holders Includes those reaching safety net
Number of patients 1 July 2019 to 30 June 2020	**1620**	**300**

Department of Veterans' Affairs health card holders are not included.

Notes

a. Your RA peer group is **Major City.**
b. Data shown are an aggregate of all your provider locations.
c. 'Your patients': patients prescribed pregabalin by you in 2019–20. Total number of prescriptions considers prescribing by any provider.
d. Prescriptions for injectable medicines, as well as those indicated solely for cancer pain, palliative care or dependence, are not included.
e. Patients may also have been prescribed opioids and/or benzodiazepines by others.

References are available at nps.org.au/pbs-pregabalin

The data are not used for any regulatory purposes and NPS MedicineWise provides this information for your reflection only. The data are from Services Australia and include medicines dispensed on the PBS for your patients.

Updating your details

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OR

Send your full name, provider number and new preferred mailing address to **provider.registration@servicesaustralia.gov.au** from a personal email address that clearly identifies you, or is the email address stored on the Medicare Provider Directory.

Would you prefer to receive your Practice Review by email?

If so please send your full name, prescriber number and preferred personal email address to **info@nps.org.au**.

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