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Gabapentinoids in psychiatric practice: *Balancing the risks and benefits*

A joint statement from:
the Royal College of Psychiatrists and
the British Association for Psychopharmacology

October 2025

POSITION STATEMENT

Joint position statement

Gabapentinoids in psychiatric practice: *Balancing the risks and benefits*

This position statement by the Psychopharmacology Committee of the **Royal College of Psychiatrists** and the **British Association for Psychopharmacology** provides clinicians with guidance on prescribing, monitoring and withdrawing from gabapentinoids safely. It aims to raise awareness of the potential risks associated with the use of these medicines, including non-prescribed use, adverse effects and withdrawal symptoms, and encourages partnership with patients.

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About this report

Purpose

This joint statement from the Psychopharmacology Committee of the Royal College of Psychiatrists and the British Association for Psychopharmacology provides a much-needed framework to support clinicians in balancing therapeutic benefit against risk in the use of gabapentinoids. It aims to:

- Remind mental health professionals of the risks associated with gabapentinoid medicines, including adverse effects, withdrawal symptoms and non-prescribed use, and raise awareness of high-risk populations
- Review the pharmacological properties of gabapentin and pregabalin, including evidence for efficacy and tolerability
- Provide an evidence-based overview of the benefits and risks of gabapentinoid use in psychiatric settings
- Highlight key considerations to support informed and cautious prescribing, monitoring and discontinuation practices and clinical decision-making, encouraging partnership with patients.

Authors and acknowledgements

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Summary

Gabapentinoids – specifically gabapentin and pregabalin – are commonly used in psychiatric settings and are frequently prescribed 'off-label' for various mental health conditions. However, gabapentin has no formal psychiatric indication and pregabalin is licensed in the UK for just one psychiatric condition: generalised anxiety disorder (GAD). (In Scotland, where gabapentinoid prescribing is more restricted, pregabalin is not routinely NHS-funded for GAD.)

Both psychological and physical symptoms of anxiety can be alleviated by gabapentinoids in some individuals; however, the clinical response is variable, and not all patients benefit. These medicines are also associated with adverse effects and a notable risk of non-prescribed use, particularly among individuals with a history of substance use disorders. In terms of withdrawing from these medications, many patients will experience distressing and severe symptoms if they are stopped abruptly.

Given these concerns, clinicians must carefully weigh the potential therapeutic benefits against the risks. Prescribing decisions should be made collaboratively with patients, emphasising informed consent, shared decision-making and strategies to prevent misuse. Caution is also essential when discontinuing treatment, and support should be provided to manage withdrawal symptoms safely.

Key messages

- Gabapentinoid medicines have a narrow range of market authorisations ('licensed use'), such as generalised anxiety disorder (pregabalin) and focal seizures (gabapentin). Yet, they are often used outside the terms of the authorisations ('unlicensed use') despite only limited evidence to support such practice.

- Non-prescribed use is common, including among patients without a history of substance misuse. Estimates suggest that among individuals using gabapentoids, as many as 1 in 10 engage in such non-prescribed use.

- Risk factors for non-prescribed use include male sex, younger age, a history of substance use disorders (especially opioid misuse), prescriptions at high dosage, and access to multiple prescribers.

- Potential harms associated with non-prescribed use of gabapentinoids include increased mortality, greater likelihood of hospitalisation and of sustaining injuries and increased risk of legal offences.

- Gabapentin and pregabalin are controlled drugs in the UK (they have been designated as Class C controlled substances since April 2019), and prescribers must comply with associated legal and regulatory requirements.

Key clinical recommendations

- Gabapentinoids should not be considered as first-line treatments for anxiety disorders:
- Use gabapentinoids only when clearly indicated, after alternative treatments have been considered.
- Avoid prescribing to patients with known or suspected substance use disorders.
- Discuss potential benefits and risks collaboratively with patients before starting treatment.
- Monitor closely for signs of misuse, including early refill requests, dose escalation and multiple prescribers.
- Withdrawal should not be abrupt; it should be done gradually and planned in collaboration with the patient.

Background and rationale

Gabapentinoids are a group of medications that are used in the treatment of a limited range of neurological and psychiatric conditions, such as epilepsy and generalised anxiety disorder (GAD) respectively. Two specific gabapentinoids – gabapentin and pregabalin – have become widely used in clinical practice. Other compounds, such as phenibut and the pro-drug of gabapentin known as gabapentin enacarbil, are only available in a few countries, and are not considered further in this statement.

Therapeutic effects

Gabapentin and pregabalin exert analgesic, anticonvulsant and anxiolytic effects. In some patients with anxiety disorders, these drugs may reduce both psychological and physical symptoms of anxiety, alleviate sleep disturbances, and improve co-occurring mild to moderate depressive symptoms. However, not all patients benefit, and some may experience adverse effects such as drowsiness and dizziness.

Licensing, funding and off-label use

Since being introduced, gabapentin and pregabalin have become two of the most commonly prescribed medicines, although often outside the narrow terms of their respective market authorisations. In the UK, it is estimated that at least half of all gabapentinoid prescriptions are for 'off-label' use.[1]

Gabapentin does not have a market authorisation ('product licence') for treating patients with psychiatric disorders in the UK, although it is licensed for the treatment of focal seizures, peripheral neuropathic pain, menopausal symptoms in women with breast cancer, oscillopsia and spasticity in multiple sclerosis, and muscular symptoms in motor neuron disease.

Pregabalin, by contrast, has a licence for in the UK for the treatment of GAD, peripheral or central neuropathic pain, and as an adjunctive therapy for focal seizures.

In England, Wales, and Northern Ireland, pregabalin is funded on the NHS for GAD, following guidance from NICE (Technology Appraisal 133), which recommends its use only when SSRIs or SNRIs are ineffective or not tolerated.

In Scotland, however, NHS prescribing of pregabalin for GAD is uncommon, as the Scottish Medicines Consortium (SMC) has not approved it for this indication. As a result, pregabalin is typically only prescribed privately for GAD in Scotland.

Non-prescribed use and dependence

Gabapentinoids are associated with the risk of 'non-prescribed use', which may involve exceeding the prescribed dose or obtaining medication from multiple sources. Risk factors for non-prescribed use include male sex, younger age and a history of substance use disorders, especially involving use of strong painkillers such as diamorphine or methadone. Non-prescribed use has been linked to increased risk of traffic accidents, injuries and fatal overdose.

Following escalating safety concerns regarding the widespread non-prescribed use of gabapentin and pregabalin (including reports of associated fatalities), these medicines were reclassified as Class C controlled substances in April 2019, with accompanying regulations regarding starting and continuing prescriptions in medical practice. Since then, further evidence has emerged highlighting the potential harms associated with non-prescribed use of gabapentinoids.[2]

Why this statement is needed

In light of the widespread use of gabapentinoids in psychiatric settings – often outside licensed indications – and the growing recognition of associated risks, this statement aims to support clinicians in making informed, evidence-based decisions about prescribing, monitoring and discontinuing these medicines. It encourages careful consideration of both the benefits and risks of gabapentinoid medication use in patients with psychiatric illness, and draws attention to the groups who may be at particular risk of problematic use.

The sections that follow summarise the pharmacological properties of gabapentin and pregabalin, review their use in psychiatric practice, highlight evidence regarding efficacy and tolerability, summarise the findings of investigations of potential harms associated with these drugs (including non-prescribed use and withdrawal symptoms), and conclude with guidance on the cautious prescribing of gabapentinoids in psychiatric practice.

How gabapentinoids work

Pharmacodynamic and pharmacokinetic properties

The gabapentinoids are substituted derivatives of gamma-aminobutyric acid (GABA) which share a common property of blocking α2δ subunit-containing voltage-gated calcium channels within the central nervous system, an effect which is most prominent after prolonged drug administration.[3]

After oral administration, gabapentin exhibits non-linear kinetics due to a saturatable transport mechanism in intestinal absorption, with decreased bioavailability at higher dosages. By contrast, pregabalin absorption is dependent upon active transport and is linear, with proportional increases in plasma levels across the dose range and maximal plasma levels occurring within 60 minutes.

Pharmacokinetic interactions with gabapentin and pregabalin are unlikely as they are not bound to plasma proteins and undergo negligible metabolism with approximately 98% of the drugs being excreted unchanged in urine.

(For an extended overview of the clinical pharmacological properties of gabapentin and pregabalin, see **reference 4** in the references list.)

Presumed mechanisms of action

Gabapentin

Gabapentin is a structural analogue of GABA but does not bind to GABA receptors or convert into GABA or another GABA receptor agonist *in vivo* and does not modulate GABA transport or metabolism.

Gabapentin is not a direct calcium channel blocker. Instead, it disrupts the regulatory function of α2δ subunits and their interactions with other proteins. It prevents delivery of α2δ subunits to the cell membrane, reduces the activation of calcium channels by α2δ subunits, and disrupts the interactions of α2δ subunits with NMDA receptors, neurexins, and thrombospondins. It inhibits GABA release and induces glutamate release from astrocytes in the locus coeruleus by an α2δ-independent mechanism; but these potentially anxiogenic effects are countermanded by increased expression of $GABA_A$ receptor expression within the hippocampus, which leads to increased tonic inhibitory conductance occurring alongside α2δ-dependent anxiolytic mechanisms.

(For additional consideration of molecular pharmacological mechanisms with gabapentin, see **reference 5** in the references list.)

Pregabalin

Pregabalin is a branched-chain amino acid, with structural similarities to L-leucine, L-isoleucine and GABA. It shows high affinity binding to the Type 1 and Type 2 proteins of the α2δ subunit of the P/Q type of voltage-gated calcium channels, mainly to α2δ-1 subunits in the cortex, olfactory bulb, hypothalamus, amygdala, and hippocampus, and α2δ-2 subunits in the cerebellum.

It does not bind directly to $GABA_A$ or $GABA_B$ receptors or to binding sites allosterically linked to GABA but increases the density of GABA transporter proteins and increases extracellular GABA in the brain through a dose-dependent increase in L-glutamic acid decarboxylase activity. Through effects on calcium channels, pregabalin administration reduces glutamate release. It may also reduce synthesis of excitatory synapses and block the 'trafficking' of new voltage-gated calcium channels to the cell surface.

(For a detailed review of probable molecular pharmacological mechanisms with pregabalin, see **reference 6** in the references list.)

Clinical use in psychiatry

Gabapentin

Gabapentin is often prescribed (outside the terms of its product licence) in patients with bipolar disorder in both short- and long-term treatment. This is possibly because of a perception that gabapentin offers anxiolytic effects without the accompanying risk of triggering hypomania or mania, which is sometimes seen with antidepressant medications.

However, evidence of its efficacy is limited.[7] A comprehensive network meta-analysis of pharmacological treatments in patients experiencing acute manic episodes found no evidence that gabapentin was superior to placebo,[8] and evidence supporting longer term use of gabapentin in patients with bipolar disorder is insubstantial.[9] Gabapentin is often prescribed to patients with anxiety symptoms but it appears to have only limited beneficial effects in small studies involving patients with social anxiety disorder or panic disorder.[10, 11]

Pregabalin

Pregabalin can be effective and well tolerated as monotherapy in patients with GAD, although adverse effects are common during both short- and long-term treatment.[12] It has broadly similar efficacy in reducing psychological and physical symptoms of anxiety and it also reduces the severity both of sleep disturbance and of co-existing depressive symptoms.[12] Augmentation with pregabalin can be beneficial in reducing anxiety symptoms after initial partial response of patients with GAD to selective serotonin reuptake inhibitors or serotonin-noradrenaline reuptake inhibitors.

Pregabalin monotherapy has also been found efficacious in acute treatment and relapse prevention in social anxiety disorder (social phobia).[13] There is some evidence that pregabalin can reduce withdrawal symptoms from benzodiazepines and zolpidem, and facilitate abstinence in previously alcohol-dependent patients.[14]

Adverse effects of taking gabapentoids

Gabapentin

The tolerability of gabapentin in short- and long-term treatment has been explored in patients with neurological, psychiatric and other conditions. A systematic review suggests gabapentin may have tolerability advantages over some other anticonvulsants in the short-term treatment of epilepsy,[15] but such advantages are not seen consistently across other conditions. The most frequent adverse effects of gabapentin treatment are dizziness and drowsiness, but fatigue, unsteadiness, nystagmus and peripheral oedema also occur commonly. Older patients may be more likely to experience adverse effects. Respiratory depression can occur when gabapentin is taken with opioids or benzodiazepines, or when used in patients with underlying respiratory illness.[16]

Pregabalin

The most reported adverse effects with pregabalin are dizziness and drowsiness (both occurring frequently in approximately 30% of patients with GAD), and less common side effects including visual disturbances, unsteadiness and clumsiness.[12] Weight gain occurs in approximately 4% of patients undergoing long-term treatment, and peripheral oedema is also reported (in less than 3% of treated patients), but does not appear to be associated with hypertension, congestive heart failure, or declining renal or hepatic function. Symptoms after abrupt discontinuation can occur, possibly less frequently than with benzodiazepines, but the incidence, severity and duration of such symptoms is not established. There are potential pharmacodynamic interactions with other central nervous system depressants and pregabalin overdose can be hazardous when combined with alcohol, benzodiazepines and opioids.[17] Furthermore, ACE inhibitors may worsen adverse effects of pregabalin, and it may enhance the fluid-retaining effect of thiazolidinedione (an anti-diabetic agent).

Pregnancy and breastfeeding

Gabapentinoids cross the placenta and are present in breast milk. Use during pregnancy or lactation should be carefully considered, weighing potential risks against clinical need. Clinicians should refer to national guidance and consult with obstetric or perinatal psychiatry services, where appropriate.

Non-prescribed use of gabapentin and pregabalin

Evidence and epidemiology

Both gabapentin and pregabalin have addictive potential and carry the risk of misuse.[18] There were few pre-clinical studies of the misuse potential with gabapentin before it became available for clinical use (in 1993). However, an early published report of gabapentin misuse[19] was followed by steadily accumulating accounts of non-prescribed usage.

A systematic review indicates that gabapentin can be taken for recreation, 'self-medication' or intentional self-harm. Patients with a history of substance misuse, especially those with current or previous opioid misuse, appear to be at particular risk.[20]

The findings of 17 pre-clinical investigations of pregabalin (including conditioned place preference and self-administration studies, typically used to assess misuse liability) incorporated within a systematic review are somewhat inconsistent. Pregabalin may have direct and indirect effects on the reward system, and so possess the potential for misuse, although it also attenuates opiate withdrawal symptoms and reduces alcohol consumption in animal models of opiate and alcohol dependence.[14]

'Euphoria' was described in approximately 5% of participants in 38 early clinical trials with pregabalin for the treatment of epilepsy.[21] Euphoria appears to be a dose-dependent effect that has been observed across indications.[19] Although often transient, its course largely remains uncertain. Supra-therapeutic doses of pregabalin can result in a sense of contentment, enhanced empathy, increased sociability, dissociation, and disinhibited behaviour.[22]

Non-prescribed use of pregabalin is reported – particularly in patients with a history of substance use disorders or after high dosage, so prescription dosage and duration should be monitored carefully.[23]

Prevalence

Early epidemiological studies of gabapentinoid use for non-medical reasons were mainly undertaken in small studies which lacked broad generalisability. However, findings from larger and more representative samples and from a series of systematic reviews[17, 18, 22, 23] indicate that the prevalence of non-prescribed gabapentinoid use is not insubstantial, although the precise extent is not established.

For example, in populations without a history of substance misuse the prevalence of non-prescribed use of pregabalin may lie between 0.5–8.5% among those dispensed

the drug.[23] Robust pharmacoepidemiological studies indicate a prevalence of prescription patterns suggestive of possible non-prescribed use of between 2–8% (gabapentin) in the United States,[24] and 6.6% (gabapentin) and 12.8% (pregabalin) in France.[25] There are marked differences between countries in the relative ratio of non-prescribed use of the two drugs, presumably reflecting local prescribing patterns.

Individuals with a history of substance use disorders are at greater risk of exhibiting non-prescribed use of gabapentinoids. To illustrate, in early cross-sectional studies pregabalin misuse was identified in 7%[26] and 12.1% of opiate-dependent patients,[27] although the six-month prevalence of gabapentinoid dependence and non-prescribed use in opioid-using individuals may be as high as 26%.[28] Opioid-using individuals may favour pregabalin over gabapentin as it reportedly confers a more rapid and stronger euphoric 'high',[17] presumably resulting from its more rapid and non-saturatable absorption, greater bioavailability, and stronger inhibitory action on $\alpha 2\delta$ subunits[4].

Risk factors

A range of risk factors associated with non-prescribed use have been identified. Individuals with a history of substance use disorders are at greater risk, particularly those with a history of opiate use[22, 23] or poly-substance use.[17] This may be because gabapentinoids might reduce opioid withdrawal syndromes,[27,28] or are being used as alternatives as the availabilities of opioids and benzodiazepines decline[29, 30] or to potentiate the effects of methadone or buprenorphine.[27, 28, 31, 32, 33] Other possible risk factors for non-prescribed use include younger age and male sex,[34] a diagnosis of anxiety,[24] access to multiple prescribers,[25] and physical illness, such as cancer, multiple sclerosis and neuropathy.[25]

Potential harms associated with non-prescribed use

Non-prescribed 'overuse' of gabapentin is associated with an increased risk of all-cause and drug-related hospitalisation, particularly if combined with opioids,[35] and pregabalin prescriptions in patients undergoing opioid maintenance therapy increase all-cause mortality.[36] The increased risk of death may result from greater respiratory depression, prolonged gastrointestinal transit increasing gabapentin concentration, and the delayed onset of the effect of gabapentinoids when compared to injected opioids[18] Findings from qualitative studies suggest that people misusing gabapentinoids may have a false sense of their presumed pharmaceutical safety.[37, 38, 39]

Gabapentinoid users may have increased risks of 'suicidal behaviour', unintentional overdoses, road traffic accidents, legal offences, and head/body injuries.[40] Non-prescribed use of gabapentinoids may be associated with dependence and withdrawal syndromes.[18]

A range of possible withdrawal symptoms have been reported including anxiety, insomnia, depression, headache, joint and muscle pains, lethargy, shivering, and sweating; case reports have also described agitation, disorientation, irritability and seizures.[18] Possible neonatal withdrawal syndromes have also been described.[41, 42] The proportion of patients who experience withdrawal symptoms is not established, but agitation, confusion and disorientation occur in approximately half of cases, following abrupt discontinuation of gabapentin.[43]

Clinical management and prevention of non-prescribed use

The principles of clinical management are summarised under clinical recommendations. Awareness of potential risks should inform all aspects of clinical practice. Mental health professionals should not regard gabapentinoids as benign anxiolytics and should act to prevent gabapentinoid misuse through careful risk assessment, counselling regarding potential risks associated with treatment prior to the first prescription, cautious prescribing, and concerted monitoring for signs of misuse.[18]

Alternatives to gabapentinoids such as psychotherapeutic approaches and differing medication classes should be considered. Clinicians should carefully consider the potential harms when contemplating the prescription of gabapentinoid medicines and remain vigilant for signs of increasing use or diversion of prescriptions. Potential indicators include requests for specific drugs or higher daily dosages, obtaining prescriptions from multiple providers, and reports of lost medications.[26] It is essential that clinicians adhere to national regulations regarding gabapentinoid prescriptions.

Prevention measures of non-prescribed use include limiting the prescriptions of gabapentinoid medicines, cautious prescribing for non-licensed indications, and the effective management of underlying conditions with other treatment approaches. There is some pharmacoepidemiological evidence that designation of gabapentinoids as Class C controlled drugs has reduced the number of new prescriptions for gabapentin and pregabalin in the UK.[44]

Patients with current psychiatric illnesses, especially substance use disorders, may be at increased risk of non-prescribed usage of gabapentinoid medicines. Clinicians should be aware that some patients might report or overstate symptoms to obtain new or renewed prescriptions or higher doses of gabapentinoids.[22]

Clinicians should also periodically review whether there is a continuing need for treatment. It has been suggested that there is a role for standard screening for non-prescribed use of gabapentinoids in patients with other substance use disorders,[46] particularly those patients with opioid use disorders.[22]

Managing withdrawal

- There is currently much uncertainty about optimal approaches for managing withdrawal from gabapentinoid medications. For example, there is no clear evidence that benzodiazepines or other adjunctive treatments[45, 46] can aid withdrawal.[47]

- In the UK, national guidance warns against abrupt discontinuation, recommends step-wise linear dose reductions, and emphasises the importance of the rate of withdrawal being agreed between patient and doctor.[48]

- Liquid formulations of gabapentin and pregabalin are available (although not universally). These allow for more precise and flexible adjustments, particularly at lower doses where tablet strengths are too large in some cases to allow small, gradual dose reductions.

- A 'hyperbolic tapering' strategy – where the dose is reduced in progressively smaller increments – may be beneficial when discontinuing gabapentinoids,[49] although there is currently little robust evidence for adopting that approach with this specific class of drugs.

Clinical recommendations

We recommend that clinicians follow these key clinical principles:

Clincal management of gabapentinoids in psychiatric practice

- Before initiating gabapentinoid treatment, consider alternative options – including non-pharmacological approaches (e.g. psychotherapy) and other medication classes.
- Be aware that gabapentinoid medicines carry the risk of non-prescribed use.
- Stay alert to patient-related risk factors associated with non-prescribed use, which include:
  - male sex
  - younger age
  - history of substance use disorders.
- Avoid prescribing gabapentinoids to patients with current or previous alcohol or substance use disorders.
- Warn patients about potential harms before and during gabapentinoid treatment.
- Follow legal requirements about limiting the treatment period and stipulating the dosage of renewed prescriptions.
- Review patients regularly to ascertain whether there is a persistent need for continued treatment.
- Monitor patients carefully but sensitively for signs of dependence and indicators of non-prescribed use.
- Support patients who develop problems associated with gabapentinoids whilst reducing and withdrawing from treatment:
  - Advise and warn patients against stopping treatment abruptly
  - Encourage patients to strengthen their support network
  - Reduce dosage at a rate agreed with the patient
  - Consider switching to liquid formulations, where available, to facilitate dosage tapering
  - Review progress regularly during the process of withdrawal.
- If initial approaches do not help, refer patients to colleagues with greater expertise in the management of non-prescribed use and treatment withdrawal.

Conclusion

Gabapentinoid medicines, while effective for many patients with certain psychiatric or neurological conditions, carry the risk of a range of adverse effects and the potential for non-prescribed use. They should not be regarded as first-line pharmacological treatments in patients with anxiety disorders – and their use should be reserved for situations where patients have not responded to initial psychological or pharmacological treatments.[50]

As awareness of the risks associated with gabapentinoids increases, perception of their overall risk–benefit profile is evolving. Clinicians should exercise caution around prescribing gabapentinoid medicines, especially when patients are known to have risk factors for non-prescribed use.

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