

Pharmacology

Gabapentin and pregabalin in the pain setting: All you need to know

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Abstract

The last decade has seen a marked increase in the use of gabapentinoid drugs for pain management. This, in part, reflects the shift from some non-steroidal anti-inflammatory drugs (NSAIDs), as well as issues arising from the protracted use of opioids. More extensive use of gabapentin and pregabalin, has seen the clinical role widen to incorporate a range of unlicensed pain scenarios, as well as increased medicines' costs.

The evidence for efficacy in some pain conditions, namely post-herpetic neuralgia and diabetic neuropathic pain, is stronger than for non-neuropathic pain conditions, such as fibromyalgia. Anxiolytic properties, as well as widespread availability, have encouraged recreational misuse, which is associated with doses outside the therapeutic range.

Safe use for neuropathic pain (central and peripheral), complex pain, migraine, and the evidence for some non-neuropathic pain conditions will be discussed, as well as the emerging abuse issues. Anti-convulsant interventions will not be covered in this article, nor will use in children.

Key words: Gabapentin; pregabalin; neuropathic pain; adjuvant pain drugs; misuse

Originally licensed as anticonvulsants, the gabapentinoid drugs, namely gabapentin and pregabalin, have become popular agents in the pain setting. Known as adjuvant pain medications, because their primary class of action is not as analgesics, prescriptions for these drugs have increased exponentially in the UK, by 150% (gabapentin) and 350% (pregabalin) between 2011 and 2016 (Spence, 2013; Iverson, 2016).

Traditionally, the main use of gabapentinoids has been for the relief of neuropathic pain, and, in the context of licensed use, specifically peripheral neuropathic pain (gabapentin) and peripheral and central neuropathic pain (pregabalin) (Joint Formulary Committee, 2018). Gabapentin was licensed as an

anti-epileptic in the UK in 1993, and pregabalin in 2004 (Morrison et al, 2017).

The gabapentinoids act by inhibiting calcium currents on central nervous system (CNS) pre-synaptic neurons, suppressing nerve signalling. While there is no proven direct effect on the inhibitory neurotransmitter GABA, there are putative effects on many neurotransmitter systems, including GABA and the monoamines (Eroglu et al, 2009) (*Table 1*). The ability to modulate pain pathways may be the reason why neuropathic pain responds to these drugs, while treatment with traditional analgesics has been less successful (Chen et al, 2004).

The explanation for the significant increase in prescribing for chronic pain conditions, and, in particular, the use of gabapentinoids, over the last decade, is unclear. Some increase is likely to be related to the search for alternatives to traditional pain relief options, given the safety issues associated with using many of the most common and popular analgesics, namely opioids, co-proxamol (now excluded) and drugs with analgesic activity, such as non-steroidal anti-inflammatory drugs (NSAIDs). Furthermore, marketing claims in the 1990s, promoting gabapentinoid use for unapproved conditions, such as non-neuropathic pain, may well have perpetuated the expansion of prescription use (Steinman et al, 2006). The practice of off-label prescribing appears to have taken hold, despite acknowledged violations of legal marketing boundaries (Newman, 2010; Ghinea et al, 2015) and subsequent clarification of approved indications for use. All prescribers are able to prescribe outside the licensed indications for a given drug, but it is incumbent on the clinician to have first ensured that this decision meets certain criteria. These include acceptable efficacy, no licensed alternative that is suitable, and that the decision is in the patient's best interests (Medicines and Healthcare products Regulatory Agency (MHRA), 2009). The responsibility for any greater risks to the patient lies with the prescribing clinician and appropriate counselling relating to safe use must be in place (MHRA, 2009).

Cochrane reports by Wiffen et al (2017) and Moore et al (2009) supported benefits for gabapentin and pregabalin, respectively, for post-herpetic neuralgia and

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Table 1. Potential effects of gabapentinoid drugs on neural pathways

Receptor/Target	Effect on pain	Reference
$\alpha 2\delta 1$ subunit on high voltage activated calcium channel	Reduces pain signal transmission	Gee et al (1996) Eroglu et al (2009)
Vallinoid receptor 1 (TrpV1)	Blocks sensory nerve pain transmission	Kim et al (2014)
NMDA receptor	Inhibition of the NMDA receptor blocks glutamate function	Hara and Sata (2007) Yang et al (2009)
$\alpha 2$ adrenergic receptors	Enhance descending pain inhibition Anti-allodynic effects attributed to this	Tanabe et al (2005)
Decreased release norepinephrine, glutamate, substance P	Lower levels excitatory neurotransmitters means less pain perception	Stahl (2004) Martinotti et al (2013)
Glutamic acid decarboxylase (GAD) (stimulates GABA)	By increasing levels, more GABA produced	Taylor (1997)

painful diabetic neuropathy. However, weaker evidence for other types of neuropathic pain, such as cancer nerve pain and complex regional pain syndrome was found (Wiffen et al, 2017). The mean number needed to harm (NNH) for all cause neuropathic pain, based on at least one adverse event was 7.5 for gabapentin, at a daily dose of >1200mg, although the NNH for serious events was not calculated (Wiffen et al, 2017). Pregabalin data showed a NNH for 300 mg at 6.6, representing at least one adverse event or serious adverse event (Moore et al, 2009).

Mechanism of action

Gabapentin and pregabalin are structurally related and appear to share the same mechanism(s) of action, but the full mechanism of action remains unclear. As the names suggest, these are analogues of the inhibitory neurotransmitter GABA, and although this was the rationale behind their development, they do not act on GABA_A or GABA_B receptors directly (Taylor et al, 1998). Central nervous system neurons transmit signals based on neurotransmitter types and levels at the synapse, and the degree of excitability of the nerve (propensity to propagate the signal). The extent of neurotransmitter availability relies on the influx of calcium ions, as this triggers neurotransmitter release. The calcium channel can be used as a switch. By modifying calcium flow, neurotransmitter disposal and the signal strength will increase or decrease.

Gabapentin and pregabalin both act to bind to a sub-unit on the voltage-gated calcium channels ($\alpha 2\delta$). This causes a narrowing of the channel, and ultimately decreases the amplitude of pain signals; therefore, less pain is perceived. Pregabalin binding has a stronger affinity for the channel, hence the higher potency (Jones and Sorkin, 1998) (Table 2). This suppression

of neuron signalling is non-specific, exerting general effects on nociceptive pathways. It is thought that there are differences in the pain signals arising from damaged nerves, for example an up-regulation of the $\alpha 2\delta$ calcium channel subunit in damaged nerves (Alles and Smith, 2016), compared to the signals emitted from damaged tissues. Efficacy in neuropathic pain could relate to this mechanism of action (Chen et al, 2018). It is relevant that the non-specific effects may also manifest as neurotoxic events, such as sedation, cognitive dysfunction, respiratory depression and visual disturbances (electronic Medicines Compendium, 2017; 2018).

A further consequence of gabapentinoid administration is elevated central GABA levels, which is why these drugs are useful in seizure control (Treimann, 2001). A variety of interactions with GABA systems, and modulation of other pain targets are noted, although some are based on animal models and the full picture remains speculative. Therefore, by enhancing the inhibitory effects of GABA, less excitatory glutamate is functional and lower levels of monoamine neurotransmitters are released, all of which suppress pain signalling (Cunningham et al, 2004; Bauer et al, 2010; Cai et al, 2012).

Pharmacokinetics and clinical profile

The faster absorption of pregabalin allows a rapid onset of action (Guay, 2005). Gabapentin does not follow first order kinetics because its absorption systems are saturable. In practical terms, this means that a higher dose is linked to lower bioavailability. There is no relevant plasma protein binding for either drug, a feature helpful for minimising drug–drug interactions

Table 2. Gabapentin and pregabalin: key characteristics for pain uses

Parameter	Gabapentin	Pregabalin
Indication for use (pain related only)	Peripheral neuropathic pain Migraine prophylaxis	Peripheral and central neuropathic pain
Dose range (minimum level efficacious for neuropathic pain)	1200-3600 mg/day (Wiffen et al, 2017)	300–600 mg/day (Moore et al, 2009)
Time to Cmax /bioavailability	2–3 hours/60%	1 hour/>90%
Potency	Less potent	2.8–6 times more potent
Half life	5–7 hours	6.3 hours
Metabolism	none	none
Excretion	Renal (unchanged drug)	Renal (unchanged drug)
Very common ($\geq 1/10$), or common adverse drug reaction ($\geq 1/100$ to $<1/10$)	Dizziness, somnolence and fatigue Increased appetite Peripheral oedema	Dizziness and somnolence Increased appetite Peripheral oedema
Serious adverse drug reaction (NOT exhaustive list)	Pneumonia Leucopenia Psychiatric reactions Pancreatitis Rhabdomyolysis	Psychiatric reactions Convulsions Congestive cardiac failure
Drug–drug interactions	CNS depressants, e.g. opiates and benzodiazepines (potentiation of effects)	CNS depressants e.g. opiates and benzodiazepines (potentiation of effects)
Drug–disease interactions	Diabetes mellitus Elderly History psychotic illness Mixed seizures	Conditions that may precipitate encephalopathy Severe congestive cardiac failure
Additional cautions	High risk of respiratory depression e.g. in elderly and those on CNS depressants (see MHRA warning)	
Withdrawal timeline	Over minimum one week	over minimum one week
Cost (drug tariff price) *	£3.24	£64.40

CNS—central nervous system
**Based on highest dose for neuropathic pain for one month using the cheapest option*
From: electronic Medicines Compendium (2017); Medicines and Healthcare products Regulatory Agency (2017); electronic Medicines Compendium (2018); Joint Formulary Committee (2018);

and adverse drug reactions (Johannessen Landmark and Patsalos, 2010).

One of the major advantages of this drug class is that they are not metabolised in the liver (Patsalos, 2013). This removes one of the most frequent causes of drug–drug interactions, that of phase 1 metabolism changes effected by other drugs. However, the lack of biotransformation does mean that the majority of these drugs are excreted whole by the kidneys (>98%) (Bockbrader et al, 2010). In situations where renal function is sufficiently compromised, the reduced clearance will mean less drug is eliminated

and more whole drug will circulate for longer. This has implications for toxicity and the dose should be adjusted accordingly.

Central neuropathic pain

Central neuropathic pain can occur following CNS injury, with stroke being a common cause (Bowsher, 1996). It can be difficult to distinguish from peripheral pain, since the impact on peripheral structures, such as muscle denervation, spasticity and overuse of unaffected sites, can produce pain. Clearly, these can coexist, complicating the pain-generating diagnosis

and management. Pregabalin is licensed for central neuropathic pain management and is used post-stroke, for multiple sclerosis and for pain associated with spinal cord injury (Watson and Sandroni, 2016).

Although unlicensed for central neuropathic pain, gabapentin is included in the National Institute for Health and Care Excellence (NICE) guidance, European Federation of Neurological Societies (EFNS) and the Canadian Pain Society recommendations for post-stroke central neuropathic pain (Attal et al, 2010; Moulin et al, 2014). The EFNS and the NICE guidelines for neuropathic pain do not distinguish between central and peripheral neuropathic pain (NICE, 2018a; Attal et al, 2010), hence both anticonvulsants appear in the guidelines.

A large systematic review conducted by Mulla et al (2015) suggested over-statement of many studies regarding the effect(s) of all interventions for central neuropathic pain, including for the anti-convulsants. Publication bias is also acknowledged by Finnerup et al (2015) regarding drugs used in neuropathic pain by up to 10%. They report 'modest' efficacy for gabapentin and pregabalin, at a number needed to treat (NNT) of 7.2 (5.9-9.21) and 7.7 (6.5-9.4), respectively. In clinical terms, this means that for every 7-8 patients, one will experience 50% or more reduction in neuropathic pain, when compared to placebo.

Complex pain

In common with other chronic pain syndromes, neuropathic pain can involve central sensitisation (Woolf, 2011). This can lock someone into a 'pain loop' from which it can be hard to escape, making effective treatment problematic. For example, following some cases of nerve injury, complex regional pain syndrome (CRPS) can occur, although nerve damage is not always the cause (Rockett, 2014). This atypical and chronic reaction to injury is often disproportionate to the injury level and can be severe and intractable (Rockett, 2014). O'Connell et al's (2013) Cochrane review does not recommend a drug for neuropathic pain is used in CRPS, stating the current evidence for any effective intervention is of poor quality.

A common form of nerve injury is radiculopathy, a compression syndrome originating at the 'root' of the nerve, e.g sciatic nerve, producing radiating pain. The approach is for first line drug intervention with NSAIDs and/or opioids, but if pain remains uncontrolled, an agent for neuropathic pain can be considered (NICE, 2017a). The choice includes the gabapentinoids, but no one agent is recommended as superior, selection being made on the optimal agent for the individual.

Phantom limb pain is another example of complex and severe pain, which is suggested to have a neuropathic element (Wiffen et al, 2017). For such conditions, only some people respond to the gabapentinoid drugs, which is unsurprising due to the

Box 1. Putative mechanisms for weight gain (mainly from anticonvulsant usage)

- Increased appetite
 - Food cravings
- Slowed metabolism
- Fatigue
- Water retention
- Less pain, enabling more socialising

(Jallon and Picard 2001, Domecq et al 2015)

complexity of the pain pathways and the individual responses to chronic pain. The evidence remains conflicted (Alviar et al, 2011; O'Connell et al, 2013) and a personalised approach to complex pain may be necessary.

Painful diabetic neuropathy

The strongest evidence for use is for neuropathic pain, of which painful diabetic neuropathy is a common cause (Dieleman et al, 2008). The NICE Clinical Knowledge Summaries (CKS) do not differentiate between a number of different drug classes as first-line interventions, allowing the clinician to select the most appropriate for the individual (NICE, 2015). However, the gabapentinoids are popular options (Rajan et al, 2014). The mean NNT is reported as 5.9 for gabapentin (Wiffen et al, 2017), and 5 for pregabalin (Moore et al, 2009), compared to placebo. Advantages include safe use with other medications, a particular benefit for the diabetic population given the frequency of polypharmacy. They are generally well-tolerated, although weight gain is a common side effect and can be an issue, with particular health implications in the diabetic population (Box 1).

Post-herpetic neuralgia

Damage from the varicella zoster virus represents one of the most painful nerve syndromes (Johnson, 2007), and is associated with burning, stabbing pain, sensory deficits, sleep disturbance and depression (Beal et al, 2012). There is a well-defined role for using the gabapentinoids for pain relief, with a mean NNT of 6.7 for gabapentin (Wiffen et al, 2017) and 3.9 for pregabalin (Moore et al, 2009). If the pain is uncontrolled with simple analgesics and practical steps such as loose clothing, NICE recommend pharmacological intervention as per neuropathic pain. No single drug on the neuropathic pain pathway is recommended over another (NICE, 2017b).

Migraine

Despite 'migraine prophylaxis' being an indication for gabapentin, this is an unlicensed use for the drug.

Box 2. Safe use of gabapentinoids

- Careful titration: start low and go slow
- Discount if not effective (usually allow at least 8 weeks for effect)
- If effective, titrate down to minimal effective level
- Counselling for benefits versus side effects and drug driving
- Warn about dependence and clarify distinction with addiction
- Check history of substance abuse
- Care if being co-prescribed with opiates
- Do not stop suddenly
- If unlicensed use, ensure patient gives informed consent.

From: National Institute for Health and Care Excellence (NICE) (2015); NICE (2018a); PrescQuipp (2016); Public Health England (2014)

Pregabalin is neither indicated, nor licensed, for use in this setting. As a cause of complex and sometimes intractable pain, migraine was one of the conditions for which gabapentin 'expanded' into trials and off-label use (Di-Trapani et al, 2000; Spira et al, 2003). However, a Cochrane review by Linde et al (2013) found that it was not an effective intervention to prevent migraine and recommended that it should not be routinely prescribed. Accordingly, the CKS pathway does not include gabapentin as a drug option (NICE, 2018b).

Fibromyalgia

The chronic pain associated with fibromyalgia is notoriously complex and multi-dimensional, but it is not classified as a neuropathic condition. In Canada and the US, pregabalin is licensed for fibromyalgia, but this is not the case for Europe. Derry et al (2016) reported that pregabalin can work for a sub-set (10%) of fibromyalgia patients to improve pain. In those who do not respond with pain relief, there may be other benefits, such as improved quality of life and function (Derry et al, 2016). The evidence for gabapentin was weaker, and Cooper et al's (2017) Cochrane review was inconclusive regarding a beneficial effect. More recent approaches to fibromyalgia include pain management programmes, which aim to place the patient at the centre in controlling their own pain (Wilkinson and Whiteman, 2017).

Acute and post-operative pain

Uses for the gabapentinoids in acute pain have emerged. There is most evidence for its use in post-operative pain. One of the areas in which prescribing has increased is following spinal surgery. Other uses have been primarily where acute pain may have an atypical or possibly neuropathic dimension, such as with burn injury. While the current literature supporting this is mostly case studies, future research may better inform clinical practice.

After surgery there is an up-regulation of calcium channels on neurons, because of the increase in cell

signal traffic (Bauer et al, 2010). This positions the gabapentinoids as a theoretically useful approach in post-surgical pain, with particular advantages for neurosurgeries, as the $\alpha 2\delta 1$ calcium channel subunit is predominantly expressed in the dorsal horn (Bauer et al, 2010). However, the effects on acute pain are controversial, as the majority of evidence is for chronic and neuropathic pain. A Cochrane review found a positive effect of gabapentin on acute pain, but an NNT of 11. While this showed that a single dose of 250 mg could reduce acute pain, it was inferior to standard NSAIDs and paracetamol interventions (Straube et al, 2010).

Other studies have shown that there is an opioid-sparing effect when using the gabapentinoids in the post-operative situation, with related advantages in reducing opioid adverse reactions, such as nausea and vomiting. This comes at the expense of the gabapentinoid adverse drug reaction profile that includes sedation and visual disturbances (Tiippana et al, 2007). It is noteworthy that no evidence supports use after surgery, to achieve prevention of chronic post-operative pain (Martinez et al, 2017). Public Health England (PHE) state that prescribing for non-neuropathic pain is not evidence-based (PHE, 2014). While acute pain represents an interesting application for these drugs, the evidence-base is mainly experimental and such prescribing is likely to be by specialist teams only.

Discontinuation

Drugs acting on CNS signalling systems exert complex effects, which are not fully understood, but it is known that certain drugs acting on these systems must be initiated and withdrawn with care (Parsons, 2018). GABA is the main fast inhibitory neurotransmitter in the CNS and is formed from glutamate, which is the main fast excitatory neurotransmitter (Huang and Thathiah, 2015). This relationship allows tightly coupled control of neural signalling, which also involves a multitude of other neurotransmitters and receptors.

As with all psychotropic drugs, neurotransmitter function(s) and signalling systems in central nervous system neuronal pathways become altered possibly because of changes to receptor expression (Cai et al, 2012). Accordingly, the regimen for use typically involves gradual adjustment to the dose, and careful titration to effective levels. If stopped abruptly, the CNS does not have the chance to re-adjust and this can lead to disruption of function around the new 'set points'. The scenarios studied for withdrawal relate to seizure control, as opposed to neuropathic pain (UK Medicines Information, 2015), making the effects of adjustment within the pain dose ranges theoretical.

Regarding GABA concentration changes, cessation can have features similar to withdrawal from benzodiazepines and alcohol, as both of these also alter

GABA function (Lobo and Harris, 2008). Withdrawal symptoms can be unpleasant, namely insomnia, irritability, headaches, gastrointestinal upset and can result in tachycardia, seizures and psychiatric reactions, such as suicidal ideation (Mersfelder and Nichols, 2016; Parsons, 2018). Occurrence of these symptoms does not represent 'addiction' to the drug, although this is a common misconception. Addiction is defined by compulsive drug-seeking behaviour and continued use, despite recognition of harm (American Society of Addiction Medicine (ASAM), 2011). It is important that this distinction is made clear to patients, in order to support safe use and concordance (Box 2).

The recommended tapering procedure is to reduce the dose over a minimum of 1 week (eMC, 2017; 2018), although the *British National Formulary (BNF)* only states this for pregabalin (Joint Formulary Committee, 2018). However, when used in the pain setting, more gradual discontinuation is helpful to monitor the effect(s) of stoppage on the background condition (PHE, 2014). PHE recommend:

- Pregabalin: reduce the daily dose at a maximum of 50–100 mg/week
- Gabapentin: reduce the daily dose at a maximum rate of 300 mg every 4 days.

If one or the other drug does not work, only partially work, or is not tolerated, it is possible to switch from one to the other. The cross-tapering protocol is approached in one of two ways. The first is to stop, using the formal discontinuation stages over at least 1 week (or longer, see above) and then to start to titrate up the alternative drug. This may allow breakthrough pain. The second is to start titrating in the other drug before full discontinuation until pain relief is established (PrescQipp, 2016).

Misuse

Greater prescription use and wider acknowledgement of gabapentinoid properties have fuelled a significant black market, abetted by online purchasing, e.g. using online pharmacies (Schifano et al, 2011). The current status as a 'prescription only medicine' and 'uncontrolled' drug group, which has not traditionally had an 'abuse' reputation, means that the gabapentinoids are excluded from the standard drug monitoring procedures. This has enabled illicit purchasing and abuse, under the radar of the authorities, both of which are particularly prevalent in the prison population and in addiction clinics (Recoppa et al, 2004; Smith et al, 2012; Baird et al 2014).

In the UK, this misuse has led to the Advisory Council for the Misuse of Drugs (ACMD) investigating the clinical and abuse roles of gabapentin and pregabalin, with a view to re-classification as controlled drugs. Growing evidence of harm has been reported from the increased number of deaths citing these drugs (1 and 4 in 2009 to 26 and 38 in 2014,

respectively (Office for National Statistics, 2016), as well as rising emergency department admissions (Millar et al, 2013). The latest information in Spring 2018 is agreement from the Government to accept the ACMD advice to re-classify pregabalin as a class C drug, after analysis from the public consultation has been completed (Iacobucci, 2017).

The characteristics of the gabapentinoids that encourage misuse include the ability to mix with many other medical and recreational drugs, such as alcohol, opioids, cannabis, selective serotonin reuptake inhibitors and amphetamines (Smith et al, 2012; Smith et al, 2016). When mixed, the potential for harm is significantly increased, causing sedation, respiratory failure and death (Lyndon et al, 2017). Both gabapentin and pregabalin can produce relaxation and elevated mood and, if crushed and inhaled nasally, can produce a 'high' similar to cocaine (Schifano et al, 2011). Furthermore, both may be used to potentiate the effects of methadone (Baird et al, 2014) and are used as cutting agents for heroin (Smith et al 2012).

Pregabalin was made a scheduled drug in the US in 2005 (schedule V), reflecting its higher abuse potential. This is probably related to its greater potency and there being a faster onset of action (Häkkinen et al 2014). There are calls for gabapentin to be 'scheduled' in the US too, particularly following a systematic review by Smith et al (2016) looking into gabapentin abuse in the US and Europe. Findings included a general population misuse rate of 1%, but this increased up to 65% for people with other prescriptions. The review found a strong relationship between opioid use (Wilens et al, 2015) and alcohol use (Häkkinen et al, 2014; Schifano et al, 2011) and gabapentin. Certainly, in the UK, it is already recommended that these drugs are only prescribed to people with a history of substance abuse, after the benefits and risks have been carefully considered (PHE, 2014). For this group, the preferred first line agent for neuropathic pain is amitriptyline (PrescQipp, 2016).

Perhaps ironically, pregabalin is also used to help manage alcohol, benzodiazepine and narcotic withdrawal (Oulis et al, 2012; Freynhagen et al, 2016), because a number of its effects relate to suppression of neuronal excitability. The very properties that make it suitable for a range of psychiatric and neurological conditions, also make it subject to abuse. It should be noted that the doses applied for medical use are effective within the therapeutic range, permitting intervention with a low risk of harm or abuse. Indeed, within dose range, and as monotherapy, these drugs are considered safe.

Conclusion

There is strong evidence to support the use of the gabapentinoids for two common neuropathic pain conditions: painful diabetic neuropathy and post-

herpetic neuralgia. Clinical efficacy is less certain for other types of neuropathic pain and caution should be exercised, even for other causes of pain either known, or perceived to be, neuropathic. There is a lack of compelling evidence for all other uses and the local pain pathway and up-to-date guidelines should be consulted, to ensure prescribing conforms to current best practice.

In view of the unlicensed status for other pain uses, and the potential for harm, clinicians should be fully aware of the relevant accountabilities in such scenarios. Exemplary counselling and support during use should help minimise safety issues. The growing misuse of this drug class is likely to focus clinical usage in the near future and it is clear that those with a history of recreational misuse (of any drug class) should avoid these drugs. Approaches to chronic pain management are slowly changing and the trend towards viewing complex pain through a non-pharmacological lens is growing, particularly as the harmful aspects of drug interventions are exposed.

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Key Points

- There is satisfactory evidence that gabapentin and pregabalin can be used as effective interventions for certain types of neuropathic pain, mainly painful diabetic neuropathy and post-herpetic neuralgia
- Due consideration must be given to prescribing gabapentin or pregabalin for off-label uses
- A detailed understanding of initiating, using, and stopping these drugs is required for safe practice
- The propensity for misuse must form part of the prescribing decision-making process, as well as patient counselling
- The UK status of pregabalin is likely to change to a controlled drug in the near future

CPD reflective questions

- What are the properties of gabapentin and pregabalin which make them useful for treating neuropathic pain?
- What are the properties of gabapentin and pregabalin which make them attractive for misuse?
- What areas of safety netting are going to be important to consider when prescribing these drugs?
- Why has it become popular to prescribe outside of the licensed indications for use?
- What will you consider discussing with patients before initiating these drugs?
- Why is it important to avoid abrupt withdrawal?

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