



Pregabalin and Gabapentin



The risks - advice for clinicians

What are Pregabalin and Gabapentin?

They are licensed to treat:

- General anxiety disorder (not first line)
- Neuropathic pain
- Focal epilepsy only (when under the care of a epilepsy specialist). Not recommended in other forms of epilepsy.

Advice to clinicians - gabapentinoids and patients with opioid dependency

- Have a gabapentinoid policy within your organisation to ensure prescribing consistency
- Be aware of licensed indications
- Be aware of the risk of respiratory depression and death when prescribing gabapentinoids, especially alongside other CNS depressants such as opioids, in the elderly, or those with respiratory/renal/neurological conditions
- Exercise extreme caution when prescribing gabapentinoids in those patients who abuse opioids or are on opiate substitution therapy and only prescribe by exception and document rationale
- Advise patients of the undesirable side effects
- Taper gradually, advising patients of withdrawal side effects
- Provide patients with a documented treatment reduction plan and review regularly. Offer psychosocial support in a collaborative manner
- Give harm reduction advice where appropriate
- Advise patients to carry naloxone if they are co-prescribed or co-use opioids, particularly if they are at increased risk of opioid overdose, to help reverse opioid toxicity.

Markers for potential misuse of gabapentinoids

- Requesting pregabalin/gabapentin specifically as treatment
- Early request for prescriptions
- Requesting replacement for lost prescriptions
- Self-increasing dosages/frequency
- Acquisition of prescriptions from alternative sources
- Minimal interest in the diagnosis or further diagnostic tests of alternative treatments/medications
- Worsening mental health presentation
- Persistent complaining
- Reporting unintended psychotropic effects from prescribed medication
- Prescription forgery
- History of substance abuse
- If these markers present, review medication carefully and consider changing to an alternative, seeking advice where appropriate.

Why do we worry about them?

- Deaths involving pregabalin or gabapentin have increased drastically in the last 10 years. In 2012, there were 12 deaths involving gabapentinoids in England and Wales, compared to 576 deaths in 2022
- ONS data from 2018 describe 272 deaths involving Pregabalin or Gabapentin in England and Wales. 230 of these deaths (85%) also mentioned an opioid
- Misuse is more marked in those with a substance misuse disorder
- Gabapentinoids have similar pharmacological effects as the inhibitory neurotransmitter GABA. This produces effects similar to alcohol/ gamma hydroxybutyrate (GHB)/benzodiazepines leading to feelings such as euphoria, dissociative effects, relaxation/calmness and psychedelic effects
- Pregabalin has a quicker absorption rate and it has over 90% bioavailability at any dose making it the more desirable of the two medicines for misuse
- It is therefore not unexpected these are sought after medications and have become a commodity
- They pose further danger due to the potentiating effects of opiates, pregabalin and gabapentin and can cause drowsiness, sedation, respiratory depression, and in extreme cases death
- There is evidence that the addition of pregabalin or gabapentin to those receiving opioids was associated with a substantially increased risk of opioid-related death
- Pregabalin use in pregnancy increases risk of physical birth abnormalities.

Tapering and withdrawal

- The summary of product characteristics suggests that both drugs can be discontinued over one week. Public Health England suggest a more gradual dose taper allows observation of emergent symptoms
- Pregabalin: reduce the daily dose at a maximum of 50-100mg/week
- Gabapentin: reduce the daily dose at a maximum rate of 300mg every four days
- Clinical judgement should be used, considering individual patient factors. If reduction rates are too difficult to achieve, prescribers should consider tapering more slowly e.g. smaller weekly decrements or monthly reductions to enable better support and encourage engagement
- Advise patients of usual withdrawal symptoms, which include; feeling anxious, insomnia, sweating, body aches, restlessness, nausea, withdrawal seizures (in epilepsy—avoid abrupt withdrawal). Patients describe this withdrawal as a difficult detox and so offer psychosocial support and reduce in a collaborative manner. See British National Formulary for more information.