Misuse and Abuse of Pregabalin

“Current Issues in Prescription and Over the Counter Medicine Abuse, Misuse and Dependence.”

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Gabapentinoids

Pregabalin and gabapentin are frequently discussed together, usually under their group name ‘gabapentinoid’. This is because they are a similar type of drug, both cited as having a risk of misuse or dependency.

They are structural analogues of the neurotransmitter GABA. Pregabalin and gabapentin are often referred to regarding their ‘off label’ use, in terms of being prescribed (or used) for a condition outside the terms of its original product authorization, or in different doses, or to patient groups not specified in the authorization.

For example, avoiding prescribing an opioid/for chronic pain.
Pregabalin and Gabapentin

**Pregabalin** is a prescription-only drug, licensed in the UK to treat epilepsy (antiseizure), neuropathic pain (pain relief) and generalised anxiety disorder (anti-anxiety). In the US it is also licensed to treat fibromyalgia.

A common brand name for pregabalin is **Lyrica®**.

**Gabapentin** is a prescription-only drug, similar to pregabalin, and prescribed for epilepsy (anticonvulsant) and neuropathic pain (pain relief).

A common brand name for gabapentin is **Neurontin®**.
Rise in Prescribing

In Europe since 2008, a significant increase in the prescribing rate for both pregabalin and gabapentin is observed.

In the UK, between 2004 and 2015, a 24% increase in the prescribing rate of gabapentinoid drugs was recorded, with a 46% rise in prescribing of gabapentin and 53% rise in pregabalin prescribing recorded since 2011.

In 2015, more than 1,800 inmates of prisons in England and Wales were prescribed gabapentin or pregabalin. This represents 3% of prison population and is twice the rate of prescribing in wider community.
Warnings of Abuse Liability

In 2005, the US made pregabalin a **controlled drug** due to the recognition of the potential risk of misuse and/or dependence.

In Europe since 2008, **concerns** about risk for misuse of or dependence on pregabalin and gabapentin are evident.

A retrospective analysis of German data showed that as early as 2008 cases of pregabalin misuse/dependence were reported.

In 2009, pregabalin and its potential involvement in **drug related deaths** in Finland, Sweden and the UK was reported to the EMCDDA Early Warning System.
Drug Effects

Pregabalin and gabapentin have a similar mechanism of action, and are reported to stimulate feelings of **sociability, euphoria, calm and relaxation.** Some users report a **stimulant** effect. Both can **enhance psychoactive effects** of other drugs. Both gabapentinoids stimulate **CNS depression,** potentially causing drowsiness, sedation, respiratory depression and death.

The pharmacokinetic properties of pregabalin contribute to it being more dangerous than gabapentin in high doses. Both are excreted unchanged in the urine.
Misuse and Pharmacokinetics

Both are misused at many multiples of therapeutic ranges, at supratherapeutic doses. Pregabalin appears to have a greater potential for misuse because of its more rapid absorption and potency. Gabapentin is absorbed more slowly and has a lower bioavailability. Plasma concentrations increase more rapidly and linearly with increasing doses in pregabalin, when compared with gabapentin.

Their CNS depressant effects may be additive with other CNS depressant drugs. Morphine can increase bioavailability of gabapentin.
Poly Use with other Drugs

**Harms:** Both drugs have *additive effects* when used with other centrally acting drugs, especially opioids. It reinforces the opioid effect.

**High dose** use of both drugs is reported, particularly within poly drug taking repertoires, particularly opioids. People who misuse opioids appear to use gabapentinoids, in particular pregabalin, to achieve a quicker euphoric high and reduce withdrawals.

**Diversion**
Risk of Overdose

Potential risks of serious side effects are greater for pregabalin than for gabapentin, although fatal overdose from either alone is thought to be very rare.

Fatal overdoses related to gabapentinoids, mostly pregabalin, in combination with other drugs are increasing in the US, Finland, Sweden, Ireland, Germany and the UK. In the US where pregabalin is controlled since 2005, gabapentin is more commonly implicated in fatal overdoses.
Prevalence and Risk Populations

Problem drug users and prison populations.

Prevalence of gabapentinoid misuse among opioid substitution treatment clients varies from 3% to 68%.

Higher prevalence of misuse among psychiatric patients and within prisons.

Implications for pain management.
User Insights from Jordan

At first it makes you sleepy, and then it elevates your mood and boosts your energy. But when you start to take 5–6 pills at once, you don’t feel sleepy, you feel active and energetic.

It (pregabalin) dissociates you from reality, you would feel normal, happy without any worries.

I started with Lyrica® at a dose of 300 mg. First, I used to take 3–4 pills, then one strip. The highest dose I took was 28 pills of Lyrica®, at one time, I mean two strips.

The worst part is that I lost everything. I no longer have confidence in myself. My whole thinking was devoted to the idea of getting money to buy Lyrica®


Risk of Dependence

Users experience **tolerance** and subsequent **withdrawal** symptoms on cessation of use of pregabalin and gabapentin. This is less common for those who use gabapentin.

Dependence on pregabalin is more common than gabapentin. There are very **few documented cases** of dependence (in contrast to misuse) in Europe.

Dependence mechanisms are not yet well understood, possible having **direct or indirect** effects on the dopaminergic ‘reward’ system.
Treatment of Dependence

• Assessment for evidence of psychological and physical features of dependence, withdrawal symptoms and co-morbid conditions such as neuropathic pain or anxiety disorder.

• Discontinuation: tapering of pregabalin at a max rate of 50-100mg per week; and gabapentin of max rate of 300mg every four days.

• Benzodiazepines.
Warnings and Control

In 2014, the UK government issued advice for prescribers on the potential risk of misuse of both pregabalin and gabapentin. It advised caution in particular when considering prescribing a gabapentinoid to a person with a known history of drug misuse or dependence. However, this should not preclude them prescribing the medication if the benefit outweighs the risk.

In 2017, the UK government commenced the process to make both pregabalin and gabapentin controlled drugs in response to concerns raised.
Thank you for your interest.
Sources

Lyons, S. Overview on pregabalin and gabapentin. Drugnet 65, p11-12
Sources


Wockhardt UK (2017) Package leaflet: information for the user: pregabalin. Available online at: [https://www.hpра.ie/](https://www.hpра.ie/)


