



## Misuse and Abuse of Pregabalin

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

Prof. Marie Claire Van Hout

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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®**.



**Pfizer** NDC 0071-1020-01

**Lyrica®** (pregabalin) 

**20 mg per mL**  
oral solution

ALWAYS DISPENSE WITH MEDICATION GUIDE  
FOR ORAL USE ONLY  
16 fl oz (473 mL) Rx only

Store at 25°C (77°F); excursions permitted to 15° - 30°C (59° - 86°F) [see USP Controlled Room Temperature].

Dispense in light (USP), child-resistant containers.

Usual Dosage: See package insert for dosage information.

Each mL contains 20 mg of pregabalin.

Distributed by:  
Parke-Davis  
Division of Pfizer Inc.  
NY, NY 10017

MADE IN SINGAPORE

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Store at 25°C (77°F); excursions permitted to 15° - 30°C (59° - 86°F) [see USP Controlled Room Temperature].

Dispense in light (USP), child-resistant containers.

**DOSAGE AND USE**  
See accompanying prescribing information.  
Each capsule contains 25 mg pregabalin.

Distributed by:  
Parke-Davis  
Division of Pfizer Inc.  
NY, NY 10017

MADE IN SINGAPORE

**Lyrica®** (pregabalin) capsules 

**25 mg**

ALWAYS DISPENSE WITH MEDICATION GUIDE

90 Capsules Rx only

NDC 0071-1012-08 PAA068745

LOTEN: 00300711012683  
DTL/EXP:

NDC 62756-137-02

Each capsule contains 100 mg of gabapentin USP

**Gabapentin Capsules, USP**

**100 mg**

Rx only  
100 CAPSULES

PAR/1374  
PAL/1374  
100, 102030

**SUN**  
SANDOZ

GUJ/DRUGS/25/789

Batch No.:  
Exp:




**Gabapenti**

**SCARACO**  
SUN PHARMACEUTICALS

Caraco Pharmaceutical Laboratories, Ltd.  
1150 Egan McCloy Drive, Dorset, VT 05832

Manufactured by:  
**Sun Pharmaceutical Ind. Ltd.**  
Acony Plaza, Andheri-Kurla Road,  
Andheri (East), Mumbai-400 059, India.

O=C(O)C1CCC(CC1)C2CCCCC2



## 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.**

## Pregabalin Misuse and Abuse in Jordan: a Qualitative Study of User Experiences

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**Abstract** Pregabalin is currently approved for the treatment of epilepsy, generalized anxiety disorder, neuropathic pain, and fibromyalgia. A qualitative study was undertaken in Jordan, where concerns have been raised about its unlicensed availability in community pharmacies and thereby its abuse. Semi-structured interviews were conducted with all patients with a history of pregabalin use in two Jordanian addiction treatment centers. All were male patients aged 21–30 years ( $n = 11$ ). The majority was poly-drug abusers and had a previous history of substance abuse (tramadol, Captagon, synthetic cannabinoids, and marijuana). Six key themes emerged from a content textual analysis which centered on *pregabalin and other drugs*; *the pregabalin effect*; *poly-pharmacy and pregabalin intoxication*; *proliferation, patterns, and routes of administration*; *dependence and withdrawal*; and *source of pregabalin*. The study underscores the need for continued pharmacovigilance to manage and address suspected abuse, along with community pharmacist and patient education regarding abuse liability and related harms.

**Keywords** Abuse · Community pharmacy · Jordan · Pregabalin

Abuse of prescription and over-the-counter (OTC) narcotics is a global issue (Hughes et al. 1999; Casati et al. 2012). OTC medications are those that can be procured from pharmacies or other retail outlets without a prescription while prescription medications are those that cannot be dispensed unless a prescription written by a physician is available (Lessenger and Feinberg 2008). Although the sale of OTC medications from community pharmacies may help individuals to self-treat minor ailments, save time, and minimize the effort of patients and physicians, some of these medicines can be abused, which subsequently may lead to addiction (Cooper 2013). The risks of addiction to prescription and OTC medications rise when they are used in means other than prescribed (e.g., at

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# 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.



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