

ACMD

Advisory Council on the Misuse of Drugs

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Karen Bradley MP
Minister for Preventing Abuse and Exploitation
Home Office
2 Marsham Street
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14 January 2016

Dear Minister,

Re: Pregabalin and Gabapentin advice

I am writing to provide you with the advice from the Advisory Council on the Misuse of Drugs (ACMD) concerning the misuse of the compounds pregabalin ((S)-3-(aminomethyl)-5-methylhexanoic acid and gabapentin (1-(aminomethyl)cyclohexaneacetic acid.

The ACMD undertook a review of the potential harms associated with the misuse of pregabalin and gabapentin following representations received from stakeholders, most notably from Northern Ireland. In the UK, pregabalin and gabapentin prescribing has increased, respectively, by 350% and 150 % in just 5 years¹.

Initial concerns regarding the potential misuse of pregabalin were raised in 2014 by the Health and Social Care Board, who noted that the use of pregabalin in Northern Ireland was significantly higher than in the rest of the UK and highlighted growing misuse and abuse.

In 2013, ten cases of recreational pregabalin abuse were presented to one Emergency Department in Belfast over the course of 2012/13.²

¹ Spence D. Bad medicine: gabapentin and pregabalin. BMJ.

2013;347:f6747.

² <http://emj.bmj.com/content/30/10/874.2.abstract>

1. Background

Description

Pregabalin and gabapentin are analogues of gamma-aminobutyric acid (GABA) but have a unique mode of action via the $\alpha_2\delta$ subunit of the N-type-calcium channel.

Known uses

Pregabalin and Gabapentin are anticonvulsant drugs with a well-defined role in the management of a number of disabling long-term conditions, including:

- epilepsy,
- postherpetic neuralgia,
- diabetic peripheral neuropathy and fibromyalgia,
- in the management of neuropathic pain, and,
- as an adjunct therapy for partial seizures.

In addition pregabalin is licensed for the treatment of generalized anxiety disorder.

Misuse

Both pregabalin and gabapentin are increasingly being reported as possessing a potential for misuse^{3 4}. When used in combination with other depressants, they can cause drowsiness, sedation, respiratory failure and death.

Pregabalin may have a higher abuse potential than gabapentin due to its rapid absorption and faster onset of action and higher potency^{5 6}. Pregabalin causes a 'high' or elevated mood in users; the side effects may include chest pain, wheezing, vision changes and less commonly, hallucinations.

Gabapentin can produce feelings of relaxation, calmness and euphoria. Some users have reported that the 'high' from snorted gabapentin can be similar to taking a stimulant⁷.

⁸In February 2015, HMI Prisons reported that health staff in a significant number of establishments continued to report high numbers of prisoners being prescribed of

³ Loftus H, Wright A. Potential misuse of pregabalin and gabapentin.

BMJ. 2014;348:g1290.

⁴ Piskorska B, Miziak B, Czuczwar SJ, Borowicz KK. Safety issues around misuse of antiepileptics. Expert Opin Drug Saf.

2013;12:647–57.

⁵ Häkkinen M, Vuori E, Kalso E, Gergov M, Ojanperä I et al (2014) Profiles of pregabalin and gabapentin abuse by postmortem toxicology, pubmed

⁶ Schifano F et al (2014) Misuse and Abuse of Pregabalin and Gabapentin: Cause for Concern? Springer Intl

⁷ <http://www.talktofrank.com/drug/gabapentin>

pregabalin and/or gabapentin, in a manner that does not meet best practice guidelines and addressing this effectively requires significant time and resource while the correct diagnosis and appropriate pain management plan are formulated.

Growing concern around the misuse of pregabalin and gabapentin has led to some organisations, including Public Health England and NHS England, writing to prescribers highlighting the potential misuse, diversion and dependence issues⁹.

The DrugScope Street Drug Survey¹⁰ (2014) reported that while illegal drugs have been increasing in purity, most areas covered by the survey highlighted the significant use of the prescription drugs pregabalin and gabapentin, chiefly among Britain's opioid-using and prison populations.

Known International use/issues

Germany: Since 2008 pregabalin abuse and dependence has been reported with increasing frequency to a German medical regulatory body (BfArM)¹¹.

Finland: The University of Helsinki has undertaken an assessment of pregabalin and gabapentin in opioid overdose deaths, noting that pregabalin abuse with high doses is increasingly common and can be fatal when combined with opioids¹.

USA: In 2005 the Drug Enforcement Administration placed Pregabalin under Schedule V of the Controlled Substances Act; citing that the abuse of pregabalin may lead to limited physical dependence or psychological dependence relative to the drugs or other substances in Schedule IV¹².

2. Harms

Medical Harms

The harms identified include:

- pregabalin and gabapentin related mortalities;
- physical dependencies.
- the propensity to cause depression of the central nervous system, resulting in drowsiness, sedation, and respiratory depression.

Fatalities

⁸ HMI Prisons **response to ACMD request for update on intelligence on the misuse of pregabalin in prisons in England and Wales, February 2015**

⁹ https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/385791/PHE-NHS_England_pregabalin_and_gabapentin_advice_Dec_2014.pdf

¹⁰ <http://www.senedd.assembly.wales/documents/s36166/HSC4-04-15%20Paper%203.pdf>

¹¹ <http://www.ncbi.nlm.nih.gov/pubmed/23292158>

¹² http://www.deaiversion.usdoj.gov/fed_regs/rules/2005/fr0728.htm

In October 2015, the National Programme for Substance Abuse Deaths (npSAD) provided the ACMD with a breakdown of deaths associated with pregabalin and gabapentin. In 2013, there were 19 deaths implicated with pregabalin and 17 deaths implicated with gabapentin in the UK (see annex 1).

In September 2015, the Office for National Statistics (ONS) released registrations information on deaths related to drug related poisoning¹³ (see annex 2). This data highlighted a significant increase in deaths from 2012 onwards. In 2014, there were:

- 38 deaths where pregabalin was mentioned on the deceased's death certificate; and,
- 26 deaths where gabapentin was mentioned on the deceased's death certificate.

3. Social Harms

The use of gabapentin and pregabalin by the opioid abusing population either together or when opioids are unavailable reinforces the behaviour patterns of this high risk population. There is a high risk of criminal behaviour stimulated by the wish to obtain gabapentin or pregabalin.

4. Interventions

The ACMD wishes to echo the recent guidance issued by Public Health England. This guidance stated that prescribing pregabalin and gabapentin for patients with a known or suspected propensity to misuse may place these people at greater risks from their use.

It should be an obligation of the prescriber to undertake a proportionate risk benefit assessment prior to the prescribing and repeat prescription of either drug.

5. Conclusions

The harms associated with pregabalin and gabapentin are commensurate with that of other substances controlled under the Misuse of Drugs Act 1971. The abuse and potential for abuse of pregabalin and gabapentin is similar to that of tramadol¹⁴, (controlled as Class C under the Misuse of Drugs Act 1971).

Pregabalin and gabapentin present a risk of addiction and a potential for illegal diversion and medicinal misuse.

6. Recommendations

The ACMD recommends that both pregabalin and gabapentin are:

- controlled under the Misuse of Drugs Act 1971 as Class C substances, and

¹³ <http://www.ons.gov.uk/ons/publications/re-reference-tables.html?edition=tcm%3A77-406863>

¹⁴ ACMD Tramadol Report (2013)

- scheduled under the Misuse of Drugs Regulations 2001 (as amended) as Schedule 3, so as not to preclude legitimate use on prescription.

Yours sincerely

A handwritten signature in black ink, appearing to read 'Les Iversen'. The signature is written in a cursive style with a large initial 'L'.

Professor Les Iversen FRS

cc Rt. Hon. Theresa May, MP, Home Secretary

Rt. Hon. Jeremy Hunt, MP, Secretary of State for Health

Jane Ellison, MP, Parliamentary Under Secretary of State for Public Health

Annex 1. Breakdown of deaths associated with pregabalin and gabapentin (2009-2013) – National Programme for Substance Abuse Deaths (2015)

Pregabalin at post mortem (braketed no. = those who were not known to be prescribed the substance)

Year of death				
2009	2010	2011	2012	2013
5	6	13	17	39
(3)	(4)	(4)	(9)	(29)

Pregabalin implicated (braketed no. = those who were not known to be prescribed the substance)

Year of death				
2009	2010	2011	2012	2013
3	3	8	13	19
(1)	(2)	(2)	(7)	(14)

Gabapentin at post mortem
(braketed no. = those who were not known to be prescribed the substance)

Year of death				
2009	2010	2011	2012	2013
10	13	18	57	30
(3)	(3)	(11)	(49)	(16)

Gabapentin implicated (braketed no. = those who were not known to be prescribed the substance)

Year of death				
2009	2010	2011	2012	2013
4	7	5	25	17
(2)	(3)	(3)	(19)	(9)

Annex 2

Table 1: Number of drug-related deaths where gabapentin and pregabalin were mentioned on the death certificate, England and Wales, deaths registered between 2009–2014;

Registration year	Gabapentin	Pregabalin
2009	1	4
2010	4	1
2011	4	4
2012	8	4
2013	9	33
2014	26	38

Office of National Statistics (2015)