



PREGABALIN

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Indications neurologiques & psychiatriques pour la Pregabaline/ Neurologische & psychiatrische Indikationen für Pregabalin quelques exemples

- la **douleur neuropathique**- Neuropathische Schmerzen
 - Derry S, Bell RF, Straube S, Wiffen PJ, Aldington D, Moore RA. Pregabalin for neuropathic pain in adults. Cochrane Database Syst Rev. 2019 Jan 23;1(1)
 - Liu L, Sun Z, Zhang Y, Ma G, Luo F. Outcomes and Predictors of Response to Pregabalin for the Treatment of Post-Traumatic Trigeminal Neuropathic Pain Following Neuroablative Procedures: A Retrospective Observational Study. Pain Physician. 2023 Sep;26(5):E539-E548. PMID: 37774191.
- la **névralgie post-zostérienne**, Neuralgie post- zoster
- la **névralgie diabétique douloureuse** – diabetische Neuropathie
- **Epilepsie focale** (comme médicament add-on dans l'épilepsie focale résistante au traitement)- fokale Epilepsie
 - Panebianco M, Bresnahan R, Hemming K, Marson AG. Pregabalin add-on for drug-resistant focal epilepsy. Cochrane Database Syst Rev. 2019 Jul 9;7(7):CD005612.

Indication psychiatrique de la Pregabalin / psychiatrische Indikation für Pregabalin

- **Anxiété généralisé/generalisierte Angststörung**
 - **CANMAD (CA 2014):** Evidence level 1
 - [BMC Psychiatry](#) volume 14, Article number: S1 (2014)
 - **S 3 Leitlinien (D 2021):** Niveau de recommandation B/Empfehlungsgrad B
 - **World Federation of Societies of Biological Psychiatry (WFSBP); 2022:**
Category of evidence A, Recommendation 1,
Evidenzgrad A, Empfehlungsgrad 1

WHO Expert Committee on Drug Dependence Information Repository (2018)



Critical Review Report:
Pregabalin

Expert Committee on Drug Dependence
Forty-first Meeting
Geneva, 12-16 November 2018

▸ **Recommendation**

- The Committee noted that there has been increasing concern in many countries regarding the abuse of pregabalin. **Cases of dependence have been reported and there are increasing numbers of reports of adverse effects. While these problems are concentrated in certain drug-using populations,** there are limited data on the extent of the problems related to pregabalin abuse in the general population. **The Committee also noted that pregabalin has approved therapeutic uses for a range of medical conditions, including some for which there are few therapeutic options.** Given the limitations of the available information regarding the abuse of pregabalin:

■ ■ Recommendation: The **Committee recommended that pregabalin ..should not be scheduled but should be kept under surveillance by the WHO Secretariat.**



Critical Review Report: Pregabalin

Expert Committee on Drug Dependence
Forty-first Meeting
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- **A lifetime prevalence of 0.25% for gabapentinoid abuse and dependence** was reported in a German geriatric non-demented hospital population (Cossmann et al. 2016).
- In the UK, found **a 0.5% self-reported lifetime prevalence of misuse of pregabalin** (Kapil et al. 2014)

Patterns of pregabalin prescribing in four German federal states: analysis of routine data to investigate potential misuse of pregabalin

	All patients prescribed pregabalin n (%) / M (SD)	Groups of patients with average doses		Unadjusted P value	Bonferroni adjusted P value
		≤600 mg/day n (%) / M (SD)	>600 mg/day n (%) / M (SD)		
Number of prescribers (practices)	1.59 (0.87)	1.57 (0.73)	2.86 (3.61)	<0.001	<0.001
Medical specialty of initial prescriber					
GP	32 911 (62.0)	32 344 (62.0)	567 (64.7)	0.010	0.256
Anaesthesiology	1935 (3.6)	1908 (3.7)	27 (3.1)		
Orthopaedics	1209 (2.3)	1192 (2.3)	17 (1.9)		
Neuroscience	4292 (8.1)	4223 (8.1)	69 (7.9)		
Neurology	5039 (9.5)	4984 (9.6)	55 (6.3)		
Psychiatry and psychotherapy	2341 (4.4)	2289 (4.4)	52 (5.9)		
Other	5322 (10.0)	5232 (10.0)	90 (10.3)		
Proportion of specialists among	0.31 (0.40)	0.31 (0.40)	0.31 (0.38)	0.300	1.000

n: first published as 10.1136/bmjopen-2021-060104 on 25

Among the 53 049 patients prescribed pregabalin, **about 2% (877) were classified as potentially misusing pregabalin.**

The majority of this group was male and aged between 30 and 60 years. **Of the patients misusing pregabalin, 365 (42%) had a diagnosed history of substance use disorders and 359 (41%) had another drug with addictive potential (opioids) before.**



Table 2 Descriptive statistics of the data set and results of the univariate statistical analyses

	All patients prescribed pregabalin n (%) / M (SD)	Groups of patients with average doses		Unadjusted P value	Bonferroni adjusted P value
		≤600 mg/day n (%) / M (SD)	>600 mg/day n (%) / M (SD)		
Patient characteristics					
Gender					
Male	21 004 (39.6)	20 468 (39.2)	536 (61.1)	<0.001	<0.001
Female	23 211 (39.9)	22 692 (39.9)	519 (61.9)	<0.001	<0.001
Age (years)					
12–17	22 (0.0)	22 (0.0)	0 (0.0)	<0.001	<0.001
18–29	86 (0.1)	86 (0.1)	0 (0.0)	<0.001	<0.001
30–39	1996 (3.8)	1808 (3.5)	188 (21.4)	<0.001	<0.001
40–49	4472 (8.4)	4271 (8.2)	201 (22.9)	<0.001	<0.001
50–59	9434 (17.8)	9252 (17.7)	182 (20.8)	<0.001	<0.001
60–69	9768 (18.4)	9677 (18.5)	91 (10.4)	<0.001	<0.001
70–79	20 473 (38.9)	20 319 (38.9)	154 (17.9)	<0.001	<0.001
≥80	20 473 (38.9)	20 319 (38.9)	154 (17.9)	<0.001	<0.001
Place of residence					
Urban area	23 500 (45.0)	23 413 (44.9)	440 (51.3)	<0.001	<0.001
Rural area	29 111 (55.0)	29 111 (55.0)	225 (26.7)	<0.001	<0.001
Approved indications					
Epilepsy	1968 (3.7)	1882 (3.6)	86 (9.8)	<0.001	<0.001
Generalised anxiety disorder	3068 (5.8)	2958 (5.7)	110 (12.5)	<0.001	<0.001
Neuropathic pain	39 829 (75.1)	39 249 (75.2)	580 (66.1)	<0.001	<0.001
Neuropathic pain (broad definition)	42 120 (79.4)	41 505 (79.6)	615 (70.1)	<0.001	<0.001
Multiple	3293 (6.2)	3186 (6.1)	107 (12.2)	<0.001	<0.001
None of the indications recorded in the records	9283 (17.5)	9098 (17.4)	185 (21.1)	0.005	0.135
Medical preconditions with increased risk of abuse					
Substance use disorders	6414 (12.1)	6049 (11.6)	365 (41.6)	<0.001	<0.001
Addictive disorder drug (alcohol)	43 (0.1)	41 (0.1)	2 (0.2)	0.345	1.000
Addictive disorder drug (tobacco)	2 (0.0)	2 (0.0)	0 (0.0)	1.000	1.000
Addictive disorder drug (opioids)	258 (0.5)	182 (0.3)	76 (8.7)	<0.001	<0.001
Drugs with potential for abuse					
Benzodiazepine	9665 (18.2)	9367 (18.0)	298 (34.0)	<0.001	<0.001
Opioids	23 886 (45.0)	23 527 (45.1)	359 (40.9)	0.015	0.386
Psychostimulants	288 (0.5)	263 (0.5)	25 (2.9)	<0.001	<0.001
Contemporaneous prescription of gabapentin	2973 (5.6)	2890 (5.5)	83 (9.5)	<0.001	<0.001
Prescription networks and structural characteristics					
Number of prescriptions	6.34 (3.28)	6.23 (2.91)	12.70 (10.17)	<0.001	<0.001
Number of prescribers (physicians)	1.79 (1.03)	1.77 (0.89)	3.12 (3.91)	<0.001	<0.001

Facteurs de risque pour abus: antécédents de consommation de substances psychotropes et addiction d'autres substances

Risikofaktoren für Missbrauch: Vorgeschichte von Substanzkonsum, Abhängigkeit von anderen Substanzen, vor allem Opiate

Table 2 Continued

	All patients prescribed pregabalin	Groups of patients with average doses		Unadjusted P	Bonferroni
		≤600 mg/day	>600 mg/day		
Number of prescribers (practices)	1.59 (0.87)	1.57 (0.73)	2.86 (3.61)	<0.001	<0.001
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Other	5322 (10.0)	5232 (10.0)	90 (10.3)		
Proportion of specialists among prescribers	0.31 (0.40)	0.31 (0.40)	0.31 (0.38)	0.300	1.000
Care density among physicians*	47.97 (70.61)	48.29 (70.67)	33.23 (66.43)	<0.001	<0.001
Care density among practices*	17.42 (35.77)	17.54 (35.84)	12.90 (32.76)	0.149	1.000
Maximal geographical distance (km)	6.86 (26.63)	6.71 (26.24)	15.98 (43.27)	<0.001	<0.001

*Care density was calculated as the average number of shared patients among all pairs of providers per patient and was calculated for patients with at least two prescribers (physicians/practices).
GP, general practitioner.

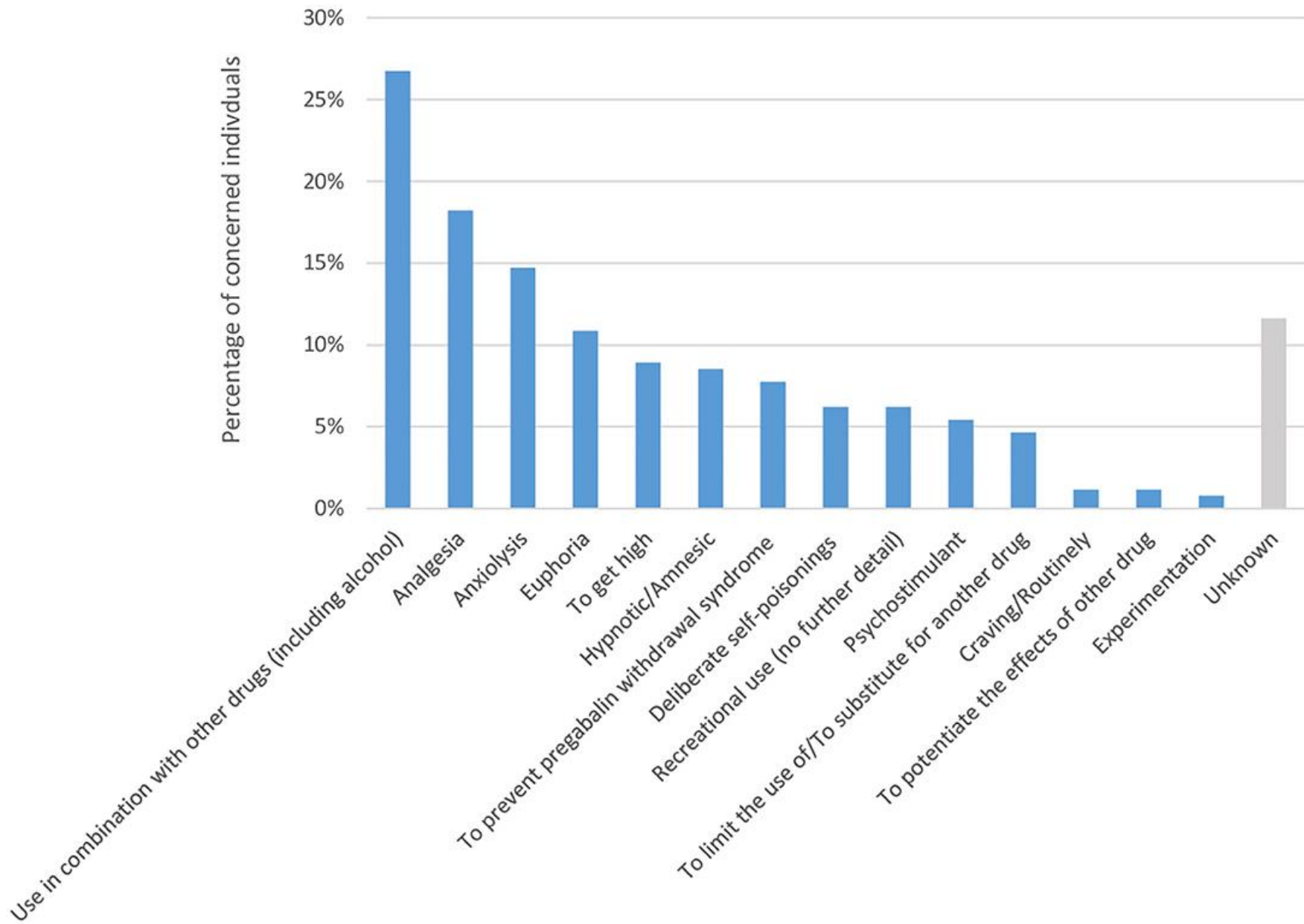
Préscription / Verschreibung: > 60% Médecins généralistes/Allgemeinmediziner

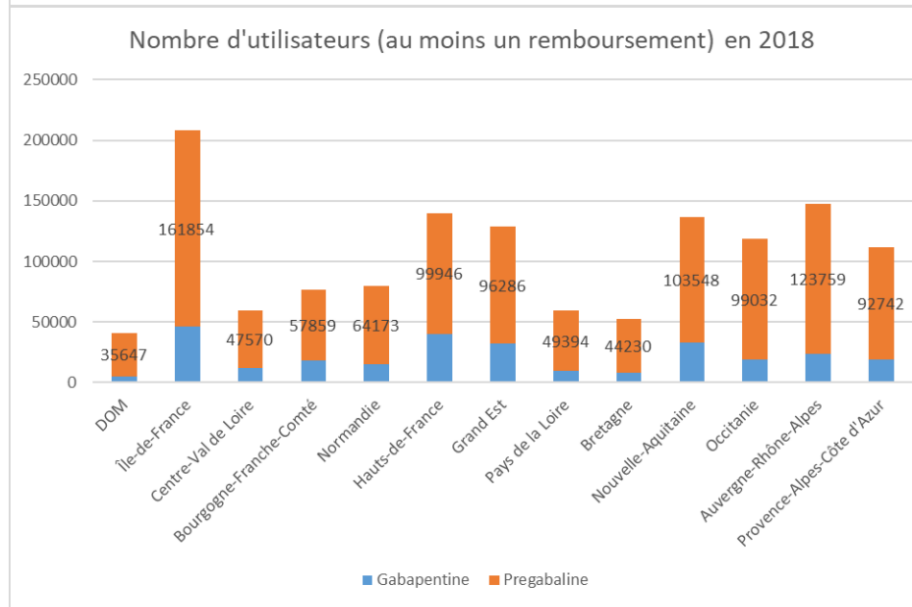
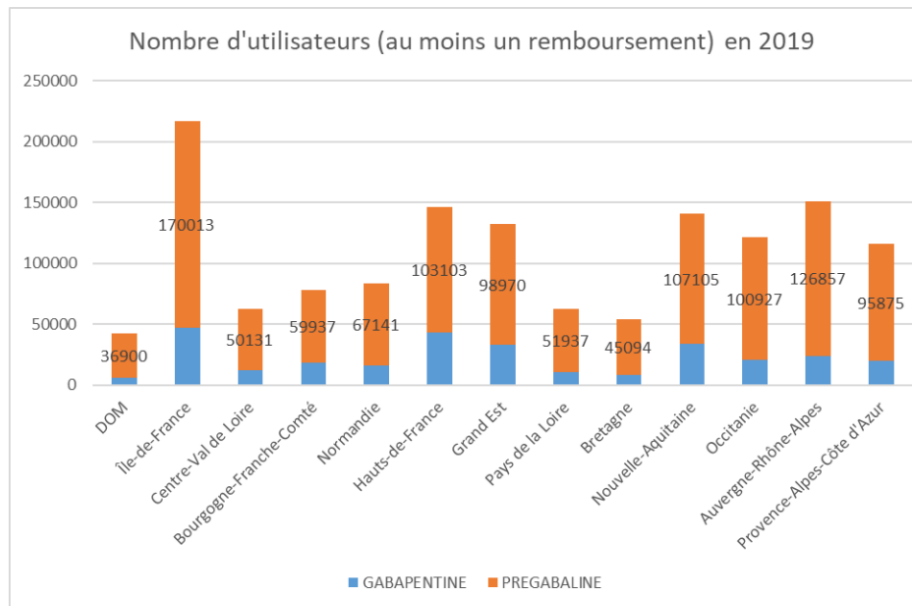
Pregabaline – situation dans d'autres pays/Situation in anderen Ländern

France:

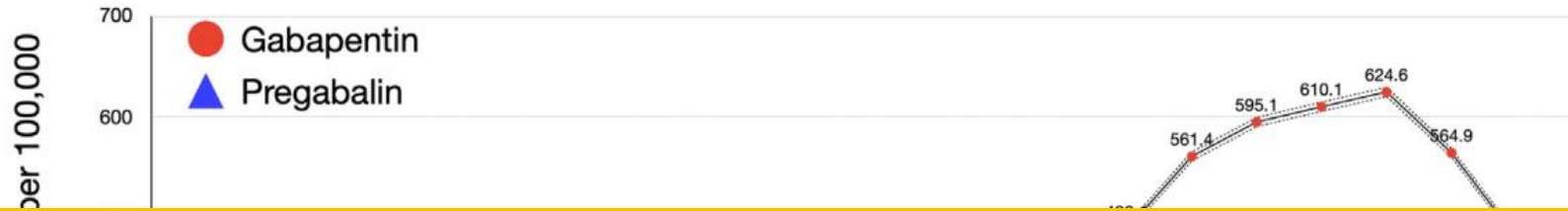
Misuse (dose > recommended dose) was more frequent in the 8692 new users of pregabalin (12.8%) than in the 1963 gabapentin (6.6%) or the 3214 duloxetine new users (9.7%) ($P < 0.001$).

- Driot D, Jouanjus E, Oustric S, Dupouy J, Lapeyre-Mestre M. Patterns of gabapentin and pregabalin use and misuse: Results of a population-based cohort study in France.

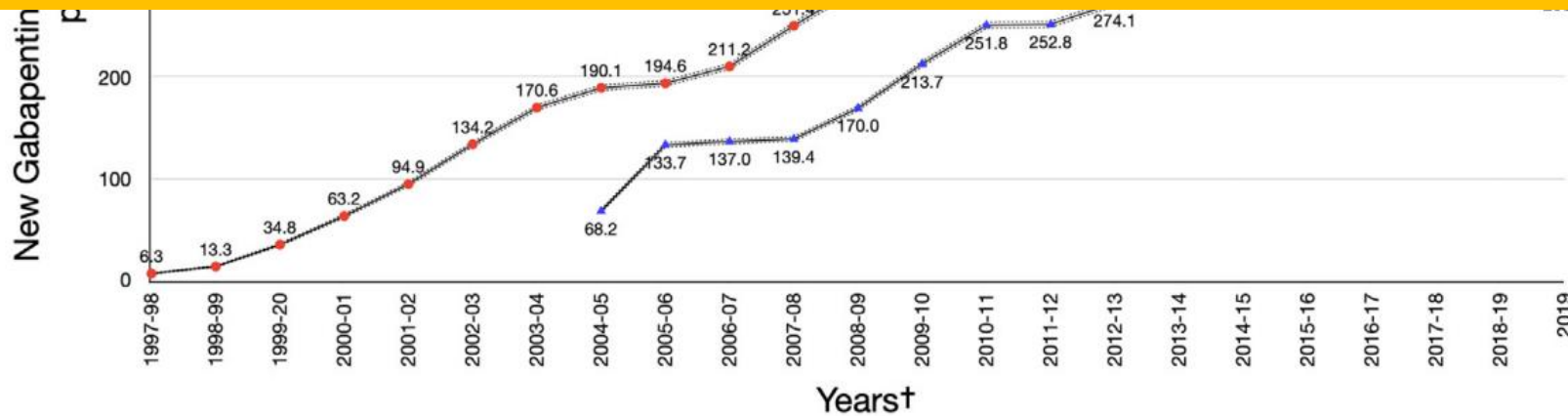




Trends in gabapentinoid prescribing in UK primary care using the Clinical Practice Research Datalink: an observational study.

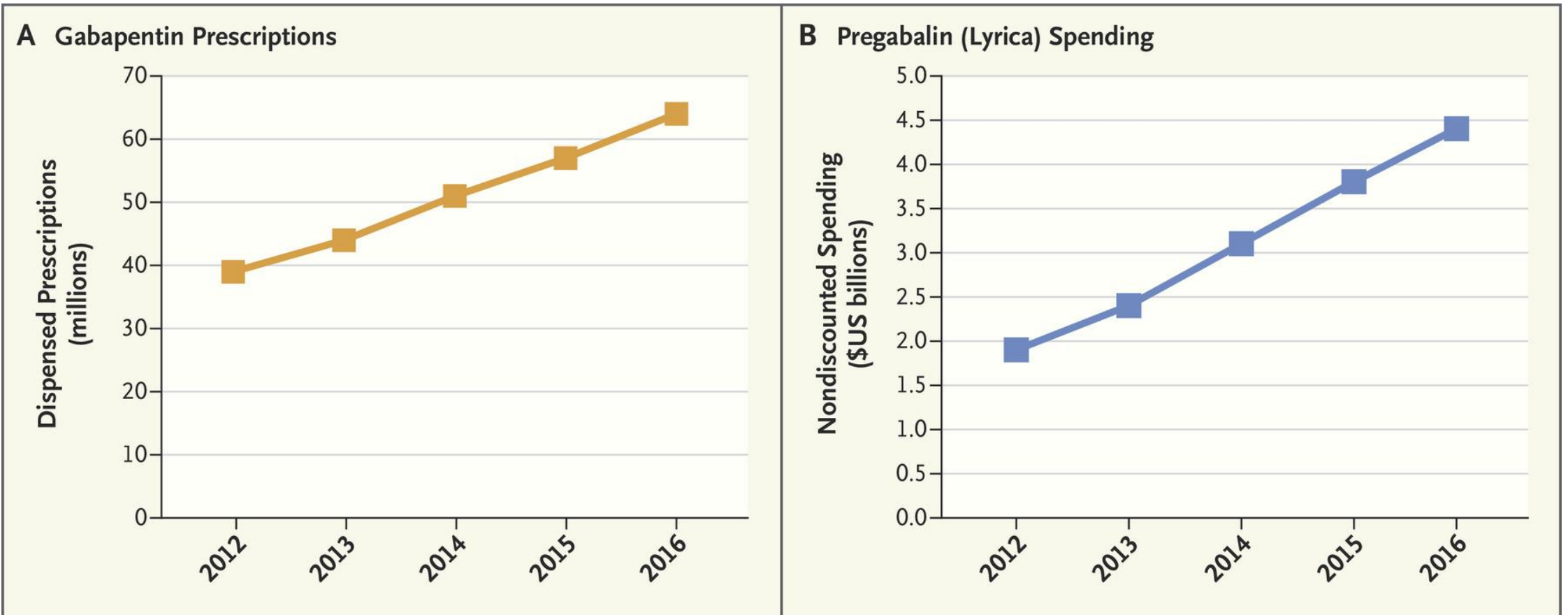


Evolution / Entwicklung UK 1997-2019
2019: Reclassification «Class C controlled substance»



† Each date range from 1997-98 to 2018-19 represents a full year (1st April to 31st March).
 2019 represents a half-year from 1st April to 30th September 2019





Dispensed Prescriptions for Gabapentin and Nondiscounted Spending for Pregabalin, 2012–2016. Data are from IMS Health.



Misuse of Pregabalin: a qualitative study from a patient's perspective

- **Semi-structured interviews with 20 participants who misuse Pregabalin** was conducted throughout the French-speaking region of Belgium
- A profile : **young male users, immigrants, mainly first generation immigrants coming from North Africa.**
- In common : **challenging or even traumatic migration pathway and precarious living conditions in Belgian territory.**
- Most of them **had no stable income.**
- **Pregabalin as a strategy to cope with their daily situation. All had psychiatric and/or somatic comorbidities for which they had apparently not received adequate medical care.** This seemed to lead many of them to use **Pregabalin as self-medication, for anxiety-depressive disorders and chronic pain,** and it was sometimes initiated in their home country. **Pregabalin was never used alone.**
- Some patients distinguished their use of Clonazepam from Pregabalin.
 - They felt that **Clonazepam would cause them more nervousness, interpersonal and legal problems and defined it as an "illegal drug",** which was not always the case with Pregabalin. **"With Rivotril, it gives problems with the police with everything. [...] It's different. It's not like Lyrica. Lyrica you eat 5,6 it's not serious in the head. Rivotril 2,3 is good. Gives you problems."** Interview 19

Potentiel addictogène / Abhängigkeitspotential

Potentiel addictogène / Abhängigkeitspotential: Pregabalin > Gabapentin

- **Préférence des consommateurs pour/ Präferenz der Patienten für pregabalin**
 - (euphorie plus rapide et plus forte- schnellere und stärkere Euphorie)
- **Pregabalin et Gabapentin effet anxiolytic avec des doses thérapeutiques**
 - Initialement stimulant, à doses plus élevés de plus en plus sédatif/ Zunahme des sedative Effekts mit zunehmender Dosis.
- **Population à risqué / Risikopopulation:**
 - Patients avec des antécédents addictologique, principalement opiacés
 - Patienten mit einer Suchtvorgeschichte, vor allem von Opiaten
- **Risque d'OD/ Risiko einer Ueberdosis:**
 - relativement secure, mais possiblement létal en combinaison avec d'autres substances psychotropes (surtout opiacés, sedatives)
 - relativ sicher, kann aber in Kombination mit Opiaten und / oder Sedativa zu letaler Ueberdosis führen
- **Arrêt / sevrage/ Absetzen / Entzug:**
 - Réduction progressive importante, sinon risque de symptomes de sevrage, même avec des doses régulières
 - Langsames und schrittweises Absetzen notwendig

Bonnet U, Scherbaum N. How addictive are gabapentin and pregabalin? A systematic review. Eur Neuropsychopharmacol. 2017 Dec;27(12):1185-1215. doi: 10.1016/j.euroneuro.2017.08.430. Epub 2017 Oct 5. PMID: 28988943.

Ishikawa H, Takeshima M, Ishikawa H, Ayabe N, Ohta H, Mishima K. Pregabalin withdrawal in patients without psychiatric disorders taking a regular dose of pregabalin: A case series and literature review. Neuropsychopharmacol Rep. 2021 Sep;41(3):434-439.

Table 4 Addictive risks of gabapentinoids and traditional substances of abuse: a comparative appraisal^a.

Characteristics/substances of abuse	Opioids	Alcohol	Gabapentin	Pregabalin	Benzodia zepines	Cannabis
Self-administration behavior (animals) "Wanting" ^a	*****	****	none	*(only on "overdose")	***	**
Physical dependence (tolerance, withdrawal symptoms)	*****	****	***	***	****	**
Behavioral = psychological dependence (craving, loss of control, addictive behavior) "Wanting" ^a	*****	*****	(*)(only in patients with history of SUD)	*(especially in patients with history of SUD)	****	***
Severity of addiction ^b	*****	****	*	**	****	***
Transitions from prescription to self-administration Wanting" ^a	*****	n/a	*	**	**	(**) ^c
Relapsing behavior/durability "Wanting" ^a	*****	*****	*	**	****	****
Voluntary treatment-seeking behavior "Wanting" ^a	*****	*****	none	none	***	***
Overdose toxicity	*****	***	*	**	****	*
Social hazards (independent on co-use of other substances of abuse) "Wanting" ^a	*****	*****	n/a ^d	n/a ^d	***	***
Rapid euphorization "Liking" ^a	***** (especially intravenous)	****	** (especially on overdose)	**** (especially on overdose)	**** (especially on overdose)	***
Easy to obtain	****	*****	****	****	****	****
Legal control of prescription/dispensing	***** (most countries)	(**) ^e	none	*(Norway, USA)	** (e.g. flunitrazepam in Germany)	***** (most countries)

The addictive power is expressed in "Wanting".

Notes:

Abbreviations: SUD = substance use disorder.

= no effects, * = very weak effects, ** = weak effects, *** = moderate effects, **** = strong effects, ***** = very strong effects. The estimation of the addictive power toxicity and safety of the gabapentinoids is based upon the present review. The estimation of the addictive power and safety of traditional drugs of abuse is based upon comprehensive reviews (e.g. [Morgan, 1990](#); [Coupey, 1997](#); [Karoly et al., 2015](#); [Korpi et al., 2015](#); [Volkow and Morales, 2015](#); [Brett and Murnion, 2015](#); [Weaver, 2015](#); [Bluth and Pincus, 2016](#); [Quednow and Herdener, 2016](#)) and the authors' expertise in the treatment of drug- and alcohol addiction (e.g. [Bonnet et al., 1999](#); [Bonnet and Gastpar, 1999](#); [Bonnet, 2011](#); [Bonnet et al., 2015](#); [Scherbaum, 2016](#)).

^aaccording to [Berridge and Robinson, 2016](#)

^baccording to the mean number of fulfilled operationalized dependence-criteria (ICD-10; DSM-IV),

^cstrong overlap between medicinal and recreational cannabis users ([Pacula et al., 2016](#)).

^dno relevant information in the literature,

^econsidering predominantly Muslim countries, laws about young people and drinking alcohol,

Regulation

- **US**

- **pregabalin** is a [Schedule V](#) controlled substance under the [Controlled Substances Act of 1970](#).^[10] (schedule I-V: V= lower abuse potential)
- ["Pregabalin"](#). The American Society of Health-System Pharmacists.
[Archived](#) from the original on December 2, 2019. Retrieved February 3, 2019.

- **UK: 2019: Class C controlled substance in the UK**

- Up to 2 years in prison, an unlimited fine or both (except anabolic steroids - it's not an offence to possess them for personal use). [Drugs penalties - GOV.UK \(www.gov.uk\)](#)
- Prescription au max. /Verschreibung max. 28 jours/Tage

Conclusion

- **Pregabalin a son utilité dans beaucoup de domaines/**
- Pregabalin ist nach wie vor nützlich (Neurologie/Psychiatrie/anesthésie)
- **Risque addictogène présent / Abhängigkeitspotential vorhanden**
- Problématique plutôt ciblée sur sous-population vulnérable, mais qui ne semble pas se mélanger avec les autres population / Problematik eher auf sub-population der Patienten (migration Maghreb, m)
- **Important: sensibilisation avec prescription rationnelle et consciente des risques/**
- Wichtig: Sensibilisierung und der Risiken bewusste Verschreibungspraxis
- **Coordination entre les acteurs au cas de mésusage/ abus**
- Koordination unter den Akteuren bei Missbrauch
- **Préscription très prudente du médicament chez des personnes dépendantes**
- Medikament sehr vorsichtig einsetzen bei Patienten mit Abhängigkeitsproblematik