Drug Enforcement Administration
Office of Diversion Control
Drug & Chemical Evaluation Section

Gabapentin (Neurontin®)

2-[1-(aminomethyl) cyclohexyl] acetic acid

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DEA/OD/ODE

Introduction:

Gabapentin is a prescription medication approved by the Food and Drug Administration (FDA) for the treatment of neuropathic pain and epileptic disorders. It is currently marketed in capsule, tablet and oral solution formulations. In recent years however, gabapentin has been increasingly encountered by law enforcement, documented in national crime lab reports, reported to poison control centers and diverted for illicit use.

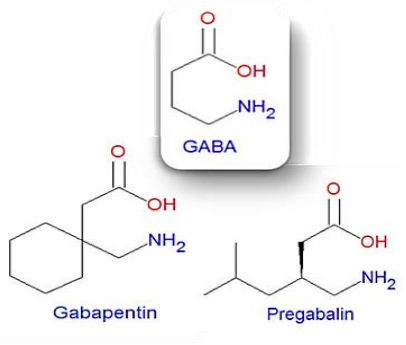
Licit Uses:

According to the FDA-approved product label, gabapentin is used clinically in the management of postherpetic neuralgia in adults and as an adjunctive therapy in the treatment of partial onset seizures, with and without secondary generalization in adults and pediatric patients 3 years and older with epilepsy.

From 2011 through 2017, annual total prescriptions for gabapentin steadily increased over two-fold from 2,965,784 in 2011 to 6,722,145 (IMS Health™). Gabapentin is available in various dosage forms and strengths including capsule strengths of 100, 300 and 400 milligrams, tablet strengths of 600 and 800 milligrams and the oral liquid form is typically produced as a 250 milligrams/5 mL solution.

Chemistry:

The chemical structures for gabapentin [1-(aminomethyl) cyclohexaneacetic acid], gamma-aminobutyric acid (GABA) and pregabalin are shown below. Gabapentin closely resembles pregabalin, a Schedule V drug under the Controlled Substances Act in its chemical structure and pharmacological activity.



The chemical structure of gabapentin is derived from the addition of a lipophilic cyclohexyl group to the backbone of GABA. Gabapentin is a crystalline substance and freely soluble in water, alkaline and acidic solutions.

Pharmacology:

The exact mechanisms through which gabapentin exerts its analgesic and antiepileptic actions are unknown, However, according to the information from the FDA approved label for gabapentin drug product, gabapentin has no effect on GABA binding, uptake or degradation. In-vitro studies have shown gabapentin binds to auxiliary α2-δ subunits of voltage-gated Ca^{2+} channels on neurons thereby resulting in a decrease in neuronal excitability.

At clinically therapeutic doses (900-3600 mg/day), gabapentin does not bind to $GABA_A$ or $GABA_B$ receptors, nor does it bind to benzodiazepine sites.

FDA-approved product label for gabapentin mentions adverse reactions such as dizziness, somnolence (drowsiness), peripheral edema (swelling), ataxia (incoordination), fatigue and nystagmus (involuntary rapid eye movement). According to a published study which analyzed online information from 32 websites, gabapentin use, similar to pregabalin, is associated with sedative and/or psychedelic effects.

Illicit Uses:

Gabapentin has been encountered in postmortem toxicology reports as indicated by data from the American Association of Poison Control Centers (AAPCC). According to the 2016 annual report of AAPCC's National Poison Data System (NPDS), gabapentin was detected in a total of 168 fatalities from 2012 to 2016. Of those cases, gabapentin was the primary cause of death in 23 individuals. Total exposure calls as a result of gabapentin increased from 5,889 in 2012 to 20,064 in 2016 for a total of 72,283. The single substance exposure involving gabapentin alone increased from 2,141 in 2012 to 7,024 in 2016. Additionally, according to the Drug Abuse Warning Network (DAWN), emergency department (ED) visit rates (per 100,000 population) for gabapentin rose from 2.7 in 2004 to 4.9 in 2011.

User Population:

In a cohort of 503 adults reporting nonmedical use of pharmaceuticals (and not enrolled in treatment facilities for such illicit use) in Appalachian Kentucky, 15% of respondents reported using gabapentin specifically to "get high". This number represented a 165% increase compared to one year prior and a 2,950% increase from 2008 respondents within the same cohort. In a 2013 online survey distributed to 1,500 respondents from the United Kingdom aged 16 to 59 years, 1.1% self-reported lifetime prevalence of gabapentin misuse.

Illicit Distribution:

STARLiMS, a web-based, commercial laboratory information management system, and the System to Retrieve Information from Drug Evidence (STRIDE), federal databases for seized drugs analyzed by DEA forensic laboratories, and the National Forensic Laboratory Information System (NFLIS), a system that collects drug analysis information from state, local, and other federal forensic laboratories contain 28 (STARLiMS and STRIDE combined data) and 2,219 reports, respectively for gabapentin in 2016. This number represents approximately a 7-fold increase from reports in 2007. Additionally, the Researched Abuse, Diversion and Addiction-Related Surveillance (RADARS) system, a prescription drug abuse/misuse and diversion monitoring system that collects geographically-specific data, indicate that 407 cases of gabapentin diversion were reported in 41 states between 2002 and 2015. The rates of diversion steadily increased from 0.0 in 2002 to 0.027 cases per 100,000 population in 2015. Published evidence also indicates that gabapentin is commonly offered for sale online from numerous websites.

Control Status

Gabapentin is not currently controlled under the Controlled Substances Act of 1970.

Comments and additional information are welcomed by the Drug and Chemical Evaluation Section; Fax 202-353-1263, telephone 202-307-7183, or E-mail ODE@usdoj.gov.