

TOP 10 FACTS

Top 10 Facts You Need to Know About Certain Aspects of Treatment with Gabapentin

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Gabapentin is approved by the Food and Drug Administration for treatment of neuropathic pain and epileptic disorders, but it is frequently prescribed off-label for a variety of other conditions, including other types of pain, anxiety, migraines, aggression associated with dementia, mood disturbances, and other disorders. The drug is widely used; in 2019, it was the 10th most prescribed medication in the United States.¹ However, there is growing concern about the use of gabapentin outside its licensed indications. This paper will discuss certain issues that have arisen regarding treatment with gabapentin.

1. Possible potential for misuse

Gabapentin has been suspected to have potential for misuse since it became widely available. The drug may be misused for euphoria, potentiating the high from opiates, reduction of alcohol cravings, a cocaine-like high, and sedation.² There are several documented cases of gabapentin misuse, dependence, and withdrawal.³ The estimated prevalence of gabapentin misuse in the general population is 1%⁴ but the estimate is much higher (15%-22%) in those with substance use disorder.⁵

Gabapentin is often misused by combining it with other substances or medications. It has been detected in combination with other substances such as opioids, tramadol, benzodiazepines, trazodone, zolpidem, stimulants, cannabinoids, and alcohol in postmortem studies.⁶⁻⁸ Misuse of gabapentin with quetiapine to achieve sedation and euphoria resulting from the combination of the two drugs has been reported in multiple persons.⁹ Gabapentin has also been used to potentiate the effect of buprenorphine/naloxone¹⁰ and methadone.¹¹

2. Closely related to pregabalin, a controlled substance

Gabapentin and pregabalin both belong to the same class of medicine (gabapentinoids) and are similar in structure. Pregabalin is classified as a Schedule V controlled substance at the Federal level.⁶ It is not unreasonable to assume that gabapentin would have some of the same clinical effects and potential for misuse as its close structural relative. The key pharmacokinetic difference is that pregabalin is more rapidly absorbed and has faster onset and increased bioavailability relative to gabapentin.¹²

Gabapentin has been classified as a controlled substance at the state level in Alabama, Kentucky, Michigan, North Dakota, Tennessee, Virginia, and West Virginia. Some states are now taking action to track gabapentin use through prescription monitoring programs.² Gabapentin is not a controlled substance in Mississippi, but prescriptions for the drug are listed in patients' Prescription Drug Monitoring Program reports.

3. Not an effective mood stabilizer

Anticonvulsants such as valproate and carbamazepine are often used to treat bipolar disorder and related psychiatric issues. However, there is minimal evidence for the efficacy of gabapentin as a mood stabilizer.¹³

4. Not the best option for treatment of anxiety and insomnia

Gabapentin is widely used off-label for treatment of anxiety disorders and insomnia.

However, results are mixed for the efficacy of gabapentin for the treatment of anxiety.¹⁴ There is minimal evidence to support the use of gabapentin for the treatment of insomnia.¹³ Pharmacological options with stronger evidence of effectiveness would be better choices.

5. Use for substance use disorders not established

Gabapentin is often prescribed off-label for treatment of substance use disorders. While there is some evidence that gabapentin may be of benefit for patients with alcohol use disorder, there is insufficient evidence to support the widespread use of gabapentin as a treatment option for alcohol withdrawal syndrome.¹⁵ There is lack of clarity about guidelines for the effective administration of gabapentin in substance use disorder treatment settings.¹⁶ Further research is needed to clarify guidelines for the use of gabapentin for substance use disorders.

6. Gabapentin and impaired driving

Gabapentin has been associated with impaired driving. A study reviewing all cases positive for gabapentin submitted to the Washington State Toxicology Laboratory between January 2003 and December 2007 revealed 137 cases of impaired driving, 7% of which were positive for gabapentin alone with the remaining 93% indicative of polydrug use. Drug Recognition Expert reports from four cases in which gabapentin was the only drug detected likely to cause impaired driving demonstrated that subjects may exhibit psychophysical indicators of a central nervous system depressant (e.g., horizontal gaze nystagmus, poor performance on standardized field sobriety tests) with clinical indicators (e.g., dilated pupils, low body temperature, and elevated pulse and blood pressure) that are not consistent with a depressant.¹⁷ Other researchers have also found several central nervous system effects associated with gabapentin misuse.¹⁸

7. Diversion of gabapentin

Limited evidence suggests that diversion of gabapentin may occur.¹⁹ A systematic review of gabapentin misuse found seven articles that mentioned or referred to diversion of gabapentin.⁶ In a cohort of 503 adults reporting use of diverted prescription opioids, 15% identified using gabapentin “to get high”.²⁰ Diversion is thought to most likely involve the opioid misuse and prison populations.²¹ Diversion of gabapentin is thus, at least, a hypothetical risk.

8. Need for screening for substance use disorders before prescribing gabapentin

Patients with a history of substance use disorders are much more likely to misuse gabapentin. Clinicians should therefore exercise caution if prescribing the drug for populations at high risk for addiction and regularly monitor for signs of misuse.^{22,23} As with other medications, patients should be advised of risks and benefits, and made aware of the potential for misuse, dependence, and withdrawal.²⁴

9. Gabapentin and breathing problems

The US Food and Drug Administration has warned that serious breathing difficulties may occur in patients using gabapentin or pregabalin who have respiratory risk factors, including the use of opioid pain medications and other drugs that depress the central nervous system, and conditions such as chronic obstructive pulmonary disease that reduce lung function. Elderly persons are also noted to be at higher risk. In clinical practice gabapentinoids are often combined with central nervous system depressants which increases

the risk of respiratory depression. There is less evidence supporting the risk of serious breathing difficulties in healthy patients taking gabapentinoids alone.²⁵

10. Suicides with gabapentin exclusively

Most cases of fatalities involving gabapentin have been found to involve other drugs, particularly opioids and benzodiazepines. Although gabapentin has a relatively safe side effect profile, one case of a death by suicide in a 62-year-old woman due solely to gabapentin toxicity has been described.²⁶

Conclusions

Gabapentin is unquestionably an effective medication for the disorders for which it has Food and Drug Administration indications. However, providers should be aware of the limited clinical evidence for use outside its licensed indications and that there is some evidence of potential misuse of the drug. Evidence suggests that some prescribers may be advocating the use of gabapentin off-label to avoid prescribing controlled substances such as opioids.²¹

It is unclear whether additional states will classify gabapentin as a controlled substance or implement additional monitoring of prescriptions for the medication, or whether the drug will become classified at the Federal level. To the best of the authors' knowledge, there are no plans for classification as a controlled substance at the state level in Mississippi. However, especially in view of gabapentin being listed on the Mississippi Prescription Drug Monitoring Program reports, this would be within the realm of possibility.

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