

CADTH RAPID RESPONSE REPORT: SUMMARY OF ABSTRACTS

Abuse and Misuse of Gabapentin: Clinical Evidence, Safety, and Guidelines

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About CADTH: CADTH is an independent, not-for-profit organization responsible for providing Canada's health care decision-makers with objective evidence to help make informed decisions about the optimal use of drugs, medical devices, diagnostics, and procedures in our health care system.

Research Questions

1. What is the clinical evidence for the potential misuse or abuse of gabapentin?
2. What are the harms associated with the potential misuse or abuse of gabapentin?
3. What are the evidence-based guidelines regarding managing patients abusing gabapentin?

Key Findings

Three systematic reviews and three non-randomized studies were identified regarding the potential abuse and misuse of gabapentin.

Methods

A limited literature search was conducted on key resources including Ovid Medline, Embase, PsycINFO, PubMed, The Cochrane Library, University of York Centre for Reviews and Dissemination (CRD) databases and a focused Internet search. No methodological filters were applied to limit retrieval by publication type. The search was limited to English language documents published between January 1, 2013 and October 2, 2017.

Selection Criteria

One reviewer screened citations and selected studies based on the inclusion criteria presented in Table 1.

Table 1: Selection Criteria

| | |
|----------------------|---|
| Population | Patients with chronic pain |
| Intervention | Gabapentin (Neurontin) |
| Comparator | No comparator |
| Outcomes | Q1-2: Misuse or abuse potential, harms, safety; Q3: Guidelines |
| Study Designs | Health technology assessments, systematic reviews, meta-analyses, randomized controlled trials, non-randomized studies, evidence-based guidelines |

Results

Rapid Response reports are organized so that the higher quality evidence is presented first. Therefore, health technology assessment reports, systematic reviews, and meta-analyses are presented first. These are followed by randomized controlled trials, non-randomized studies, and evidence-based guidelines.

Three systematic reviews and three non-randomized studies were identified regarding the potential abuse and misuse of gabapentin. No health technology assessments, randomized controlled trials, or evidence-based guidelines were identified.

Additional references of potential interest are provided in the appendix.

Overall Summary of Findings

Three systematic reviews (SRs) were identified.¹⁻³ Two systematic reviews examined the misuse potential of gabapentin,^{1,3} and one examined the safety of gabapentin for individuals with chronic low back pain.² Analysis of included studies in one systematic review¹ found that increasing numbers of patients were using gabapentin in higher than recommended doses, revealing a potential for abuse with gabapentinoid-type medications. The prevalence of gabapentinoid abuse was higher in current opioid abusers,^{1,3} and higher in individuals with a gabapentin prescription.³ Misuse of gabapentin occurred for recreational reasons, self-medication, or for intentional self harm, and was used in combination with other substances, or alone.³

In patients with chronic back pain, gabapentin can be prescribed and used in the long term. Whilst no deaths or hospitalizations occurred within one SR² in this patient group, the use of gabapentin was associated with other adverse effects when compared with placebo, including dizziness, fatigue, mentation difficulties, and visual disturbances. The relative risks of these adverse events were all significant, although the evidence base itself was judged to be of low quality.²

Three non-randomized studies (NRS) were identified,⁴⁻⁶ two of which examined gabapentin's abuse potential,^{5,6} and one of which examined patient harm associated with overuse of gabapentin.⁴ Sustained overuse of gabapentin increased odds of all-cause inpatient hospitalization, hospitalization due to altered mental status, and drug-related inpatient hospitalization.⁴ Gabapentin overuse also increased odds for respiratory depression.⁴

The authors of one NRS⁵ found that gabapentin use patterns were similar to other drugs of abuse, with the top one percent of users filling prescriptions that, on average, were over three times the recommended maximum. The authors of a second NRS⁶ found that 4.8% of misuse reports were associated with gabapentin, and the reporting frequency increased over time. There were also 86 fatalities associated with the use of gabapentin, mostly when in combination with opioids.⁶

References Summarized

Health Technology Assessments

No literature identified.

Systematic Reviews and Meta-analyses

1. Evoy KE, Morrison MD, Saklad SR. Abuse and misuse of pregabalin and gabapentin drugs. 2017 Mar;77(4):403-26.
[PubMed: PM28144823](#)
2. Shanthanna H, Gilron I, Rajarathinam M, AlAmri R, Kamath S, Thabane L, et al. Benefits and safety of gabapentinoids in chronic low back pain: a systematic review and meta-analysis of randomized controlled trials. Plos Medicine. 2017;14(8).
3. Smith RV, Havens JR, Walsh SL. Gabapentin misuse, abuse and diversion: a systematic review. Addiction. 2016 Jul;111(7):1160-74.
[PubMed: PM27265421](#)

Randomized Controlled Trials

No literature identified.

Non-Randomized Studies

4. Peckham AM, Fairman KA, Sclar DA. All-cause and drug-related medical events associated with overuse of gabapentin and/or opioid medications: a retrospective cohort analysis of a commercially insured US population. Drug Saf. 2017 Sep 27.
[PubMed: PM28956286](#)
5. Peckham AM, Fairman KA, Sclar DA. Prevalence of gabapentin abuse: comparison with agents with known abuse potential in a commercially insured US population. Clin Drug Invest. 2017 Aug;37(8):763-73.
[PubMed: PM28451875](#)
6. Chiappini S, Schifano F. A decade of gabapentinoid misuse: an analysis of the European Medicines Agency's 'Suspected Adverse Drug Reactions' Database. CNS Drugs. 2016 Jul;30(7):647-54.
[PubMed: PM27312320](#)

Guidelines and Recommendations

No literature identified.

Appendix — Further Information

Previous CADTH Reports

7. Prescribing and dispensing policies to address harms associated with prescription drug abuse. Ottawa: CADTH; 2015 Oct. (CADTH Environmental Scan)
https://www.cadth.ca/sites/default/files/pdf/ES0291_Prescription_Drug_Abuse_e.pdf
8. Gabapentin for adults with neuropathic pain: a review of the clinical efficacy and safety. Ottawa: CADTH; 2015 Apr 14. (CADTH Rapid Response Reports).
<https://www.cadth.ca/sites/default/files/pdf/htis/apr-2015/RC0637-Gabapentin-NeuropathicPain%20Final.pdf>
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<https://www.cadth.ca/sites/default/files/pdf/htis/dec-2014/RC0594%20Gabapentin%20for%20neuropathic%20pain%20Final.pdf>
10. Narcotics, benzodiazepines, stimulants, and gabapentin: policies, initiatives, and practices across Canada Ottawa: CADTH, 2014. (CADTH Environmental Scan)
https://www.cadth.ca/sites/default/files/pdf/ES0285_Narcotics_BZD_Stimulants_Gabapentin_e.pdf

Systematic Reviews – No Outcome Information in Abstract

11. Chaparro LE, Smith SA, Moore RA, Wiffen PJ, Gilron I. Pharmacotherapy for the prevention of chronic pain after surgery in adults. Cochrane Database Syst Rev. 2013 Jul 24;(7).
[PubMed: PM23881791](https://pubmed.ncbi.nlm.nih.gov/23881791/)

Non-Randomized Studies – Alternative Population

12. Smith RV, Lofwall MR, Havens JR. Abuse and diversion of gabapentin among nonmedical prescription opioid users in Appalachian Kentucky. Am J Psychiatry. 2015;172(5):487-8.
13. Wilens T, Zulauf C, Ryland D, Carrellas N, Catalina-Wellington I. Prescription medication misuse among opioid dependent patients seeking inpatient detoxification. Am J Addict. 2014 Nov 19.
[PubMed: PM25409541](https://pubmed.ncbi.nlm.nih.gov/25409541/)

Qualitative Studies

14. Buttram ME, Kurtz SP, Dart RC, Margolin ZR. Law enforcement-derived data on gabapentin diversion and misuse, 2002-2015: diversion rates and qualitative research findings. Pharmacoepidemiol Drug Saf. 2017 Sep;26(9):1083-6.
[PubMed: PM28493425](https://pubmed.ncbi.nlm.nih.gov/28493425/)

Review Articles

15. Quintero GC. Review about gabapentin misuse, interactions, contraindications and side effects. 2017; J Exp Pharmacol, 2017;9:13-21.
[PubMed: PM28223849](https://pubmed.ncbi.nlm.nih.gov/28223849/)

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[PubMed: PM26928397](#)
17. Mersfelder TL, Nichols WH. Gabapentin: abuse, dependence, and withdrawal. *Ann Pharmacother.* 2016 Mar;50(3):229-33.
[PubMed: PM26721643](#)
18. Stannard C. Misuse of gabapentin and pregabalin: a marker for a more serious malaise? *Addiction.* 2016;111(10):1699-700.
19. Evrensel A, Unsalver BO. Psychotic and depressive symptoms after gabapentin treatment. *Int J Psychiatry Med.* 2015;49(4):245-8.
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20. Perinpanayagam J, bu-Asi MJ, Bustamante S, Kunnumpurath S. Opioid-sparing drugs (ketamine, gabapentin, pregabalin, and clonidine). In: Kaye AD, editor. *Substance abuse: inpatient and outpatient management for every clinician.* New York: Springer Science + Business Media; 2015. p. 319-30.
21. Ryan NM. A review on the efficacy and safety of gabapentin in the treatment of chronic cough. *Expert Opin Pharmacother.* 2015 Jan;16(1):135-45.
[PubMed: PM25380977](#)
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[PubMed: PM24596960](#)
23. Schifano F. Misuse and abuse of pregabalin and gabapentin: cause for concern? *CNS Drugs.* 2014 Jun;28(6):491-6.
[PubMed: PM24760436](#)
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[PubMed: PM23642151](#)

Additional References

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