Misuse:

- Typically involves taking doses higher than prescribed. Reportedly results in experiences similar to opioids, benzodiazepines, and psychedelics.[14]
- Estimated to be only 1% of the general population. However, increases to 15-22% in those diagnosed with a comorbid opioid use disorder.[14]

Conclusion

- Gabapentin is a safe and well-tolerated medication to address alcohol-related PAWS.
- Given the risk of recurrence with PAWS, addressing the symptoms of PAWS can lead to better outcomes.
- Misuse should be considered in those with a history of other substance use disorders, in particular opioids.

References

1. SAMHSA. Protracted Withdrawal Symptoms. 2010;9(1): 1-8. www.samhsa.gov.
2. Miller NS, Kipnis SS. A Treatment Improvement Protocol Detoxification and Substance Abuse Treatment TIP 45 Detoxification and Substance Abuse Treatment A Treatment Improvement Protocol TIP 45. 2006. www.samhsa.gov
3. Barbara J. Mason, PhD, Susan Quello, BA, BSa, Vivian Goodell, MPH FS, MD. Gabapentin Treatment for Alcohol Dependence: A Randomized Controlled Trial. 2015;174(1):70-77. doi:10.1001/jamainternmed.2013.11950. Gabapentin
4. Martinotti G, Nicola M Di, Reina D, et al. Alcohol protracted withdrawal syndrome: The role of anhedonia. Subst Use Misuse. 2008;43(3-4):271-284. doi:10.1080/10826080701202429
5. Brower KJ. Alcohol's Effects on Sleep in Alcoholics. Alcohol Res Heal. 2009;25(2):110-125.
6. Anton RF, Latham P, Voronin K, et al. Efficacy of Gabapentin for the Treatment of Alcohol Use Disorder in Patients with Alcohol Withdrawal Symptoms: A Randomized Clinical Trial. JAMA Intern Med. 2020;180(5):728-736. doi:10.1001/jamainternmed.2020.0249
7. Schacht JP, Randall PK, Waid LR, et al. Neurocognitive performance, alcohol withdrawal, and effects of a combination of flumazenil and gabapentin in alcohol dependence. Alcohol Clin Exp Res. 2011;35(11):2030-2038. doi:10.1111/j.1530-0277.2011.01554.x
8. Myrick H, Anton R, Voronin K, Wang W, Henderson S. A double-blind evaluation of gabapentin on alcohol effects and drinking in a clinical laboratory paradigm. Alcohol Clin Exp Res. 2007;31(2):221-227. doi:10.1111/j.1530-0277.2006.00299.x
9. Myrick H, Malcolm R, Randall PK, et al. A double-blind trial of gabapentin versus lorazepam in the treatment of alcohol withdrawal. Alcohol Clin Exp Res. 2009;33(9):1582-1588. doi:10.1111/j.1530-0277.2009.00986.x
10. Bisaga A, Evans SM. The acute effects of gabapentin in combination with alcohol in heavy drinkers. Drug Alcohol Depend. 2006;83(1):25-32. doi:10.1016/j.drugalcdep.2005.10.008
11. Mason BJ, Quello S, Shadan F. Gabapentin for the treatment of alcohol use disorder. Expert Opin Investig Drugs. 2018;27(1):113-124. doi:10.1080/13543784.2018.1417383
12. Anton RF, Myrick H, Wright TM, et al. Gabapentin Combined with Naltrexone for the Treatment of Alcohol Dependence. 2011;168(7):709-717. doi:10.1176/appi.ajp.2011.10101436.Gabapentin
13. Smith R V, Havens JR, Walsh SL. Gabapentin misuse, abuse, and diversion: A systemic review. Addiction. 2016;111(7):1160-1174. doi:10.1111/add.13324.Gabapentin
14. Keyes KM, Liu XC, Cerda M. The Role of Race/Ethnicity in Alcohol-attributable injury in the United States. Epidemiol Rev. 2012;34(1):89-102. doi:10.1093/epirev/mxr018
15. SAMHSA. Results from the 2018 National Survey on Drug Use and Health: Detailed Tables. Subst Abus Ment Heal Serv Adm. 2019; (June 2020).
16. Calcaterra S, Glanz J, Binswanger IA. National trends in pharmaceutical opioid related overdose deaths compared to other substance related overdose deaths: 1999-2009. Drug Alcohol Depend. 2013;131(3):263-270. doi:10.1016/j.drugalcdep.2012.11.018
17. Mulia N, Tam TW, Schmidt LA. Disparities in the Use and Quality of Alcohol Treatment Services and Some Proposed Solutions. Psychiatr Serv. 2014;65(5):626-633. doi:10.1176/appi.ps.201300188.Disparities
18. Acevedo A, Panas L, Garnick D, et al. Disparities in the Treatment of Substance Use Disorders: Does Where You Live Matter? J Behav Heal Serv Res. 2018;45(4):533-549. doi:10.1007/s11414-018-9586-y.Disparities
19. McKnight-Eily LR, Okoro CA, Strine TW, et al. Racial and Ethnic Disparities in the Prevalence of Stress and Worry, Mental Health Conditions, and Increased Substance Use Among Adults During the COVID-19 Pandemic — United States, April and May 2020. MMWR Morb Mortal Wkly Rep. 2021;70(5):162-166. doi:10.15585 mmwr.mm7005a3

GC97277

Clinician Guide to Post-Acute Withdrawal Syndrome from Alcohol

Roberto D. Sanchez, D.O.

Ali Abbas Asghar-Ali, M.D.

VA | U.S. Department of Veterans Affairs

south central mirecc
Mental Illness Research, Education and Clinical Center

Post-Acute Withdrawal Syndrome (PAWS):

- PAWS denotes protracted withdrawal symptoms after acute detoxification from specific substances, including alcohol.[1]
- Protracted withdrawal is defined as the presence of substance-specific signs and symptoms common to acute withdrawal but persisting beyond the generally expected acute withdrawal timeframes.[1]
- Acute withdrawal from alcohol is generally 5-7 days.[1,5] with protracted withdrawal persisting outside this window.
- While there is known clinical observation and patient self-report, PAWS is not yet included in the Diagnostic and Statistical Manual of Mental Disorders due to limited research.[1]
- Symptoms are linked to increased risk of recurrence.[2–4]

Common Symptoms of PAWS:

- Anhedonia*
- Irritability
- Anxiety
- Dysphoria*
- Decreased concentration
- Difficulties with short-term memory
- Persistent fatigue
- Insomnia*
- Impaired executive control
- Unexplained pain/somatic complaints
- Cravings

**denotes symptoms that may contribute to recurrence and improve with gabapentin*

Minority Populations

- Estimates show the prevalence of substance use disorders in minority populations are generally not higher, but minorities are less likely to receive addiction treatment.[14–19]
- Consequences of substance use are disproportionally experienced by minority populations.[18]
  - Black individuals are more likely to face legal consequences related to their alcohol use disorder (AUD).[8]
  - Mortality related to AUD is disproportionately higher in Latino and Black populations.[18]

Gabapentin as a Treatment for PAWS:

- PAWS is thought to occur primarily through GABA and glutamate brain signaling.[6] As a result, gabapentin is of interest as a potential treatment.
- Gabapentin mechanism: binding at the alpha-2delta site of calcium channels and secondarily altering GABA and glutamate activity in the brain.[6]
- Majority of studies reviewed used at least 1200mg daily and not beyond 1800mg. A randomized controlled trial (RCT) found that a dose of 1800mg efficaciously treated PAWS symptoms of dysphoria, craving, and insomnia.
- No evidence for benefit beyond doses of 1800mg daily.
- An example of a titration schedule[6]:
  - Day 1: 300mg at bedtime
  - Day 2: 300mg in the morning and at bedtime
  - Day 3 and 4: 300mg in the morning, at noon and at bedtime.
  - Day 5 onward: 300mg in the morning, 300mg at noon, 600mg at bedtime.
  - At this time there are no clear guidelines for when to taper off gabapentin.
- Titration may be expedited in the inpatient setting.

Benefits of Gabapentin:

- Renal excretion; safer for those with hepatic impairment.[6]
- Fewer cognitive effects.[6,7]
- No significant adverse interactions with alcohol.[6,8–10]
- Demonstrated efficacy in improving insomnia and negative affect in PAWS.[11]

Gabapentin in Combination Treatment:

- Anti-craving medications such as naltrexone work by different mechanisms than gabapentin.
- An RCT found that combination of gabapentin and naltrexone improved drinking outcomes.[13] Outcome did not persist after gabapentin was discontinued.[13]