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IN BRIEF

Respiratory Depression with Gabapentinoids

The FDA has required new warnings in the labels of gabapentin (*Neurontin*, and others) and pregabalin (*Lyrica*, *Lyrica CR*, and generics) about the risk of life-threatening or fatal respiratory depression in patients with respiratory risk factors.¹ Respiratory risk factors include chronic obstructive pulmonary disease (COPD) and concurrent use of opioids or other CNS depressants. Elderly patients are also at increased risk.

Gabapentin and pregabalin are FDA-approved to treat a variety of neurologic and neuropathic disorders and are frequently used off-label to treat non-neuropathic pain, anxiety, and insomnia, and hot flashes in women with breast cancer.²⁻⁵ Often prescribed with opioids and other CNS depressants, gabapentinoid misuse and abuse has been increasing. Gabapentin and pregabalin have a lower potential for abuse than opioids, but physical and psychological dependence can occur.

Gabapentinoids alone can cause respiratory depression. Coadministration with an opioid can increase the risk of opioid-related death.⁶ Possible mechanisms include reversal of opioid-induced tolerance and additive respiratory depression.⁷

Starting gabapentinoids at a low dose and titrating carefully is recommended to reduce the risk of respiratory depression in patients with respiratory risk factors and in the elderly. Reductions in the dosage of gabapentin and pregabalin are necessary in patients with renal impairment. ■

1. FDA. FDA warns about serious breathing problems with seizure and nerve pain medicines gabapentin (*Neurontin*, *Gralise*, *Horizant*) and pregabalin (*Lyrica*, *Lyrica CR*). Available at: <https://bit.ly/3e8w6nK>. Accessed May 21, 2020.
2. Nonopioid drugs for pain. *Med Lett Drugs Ther* 2018; 60:24.
3. Drugs for anxiety disorders. *Med Lett Drugs Ther* 2019; 61:121.
4. Drugs for chronic insomnia. *Med Lett Drugs Ther* 2018; 60:201.
5. Oxybutynin for hot flashes in women with breast cancer. *Med Lett Drugs Ther* 2019; 61:30.
6. T Gomes et al. Gabapentin, opioids, and the risk of opioid-related death: a population-based nested case-control study. *PLoS Med* 2017; 14:e1002396.
7. R Hill et al. Oxycodone-induced tolerance to respiratory depression: reversal by ethanol, pregabalin and protein kinase C inhibition. *Br J Pharmacol* 2018; 175:2492.

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