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WHITE PAPER

FDA warns about serious breathing problems associated with Gabapentinoids

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The U.S. Food and Drug Administration (FDA) is warning that serious breathing problems have been associated with gabapentinoids such as oral gabapentin and pregabalin when used with CNS depressants or in patients who have respiratory risk factors. These warnings are based on a review of several sources of data including case reports submitted to the FDA or published in the medical literature, observational studies, human trials and animal studies. [2] Gabapentin and pregabalin are FDA-approved for a variety of conditions, including seizures, nerve pain, and restless legs syndrome.[4]

Co-misuse of gabapentinoids and opioids is particularly concerning because high-dose pregabalin may exaggerate the respiratory depression seen with opioid use. [1] Although gabapentin is widely perceived as safe, drug-induced respiratory depression has been described when oral gabapentin is used alone or in combination with other medications. [3] The mechanism by which gabapentin may increase the risk of death in opioid users likely reflects both a pharmacodynamic and pharmacokinetic interaction.[3] More specifically, it likely reflects additive respiratory depression as well as increased gabapentin concentrations with concomitant opioid use.[3]

In addition, potential risk factors for gabapentin-related respiratory depression include advancing age, renal insufficiency, chronic lung disease, and dose. [3] Also, patients who have underlying respiratory impairment, such as patients with chronic obstructive pulmonary disease (COPD).[2] Among 49 case reports submitted to FDA over the 5-year period from 2012 to 2017, 12 people died from respiratory depression with gabapentinoids, all of whom had at least one risk factor. [4]

Symptoms of respiratory problems include confusion or disorientation, unusual dizziness or lightheadedness, extreme sleepiness or lethargy, difficult breathing (or slowed, shallow), unresponsiveness (which means a person doesn't answer or react normally or you can't wake them up), bluish-colored or tinted skin (especially on the lips, fingers, and toes).[4] The gabapentinoid prescribing information already includes guidance for health care professionals to caution patients about dizziness, somnolence, and the potential for impaired ability to operate a car or complex machinery.[4]

The FDA states health care professionals should start gabapentinoids at the lowest dose and monitor patients for symptoms of respiratory depression and sedation when co-prescribing gabapentinoids with an opioid or other CNS depressants. [4] Another good option is to prescribe topical gabapentin alone or in combination with low dose oral gabapentinoids. Topical application seemed to largely circumvent the more common systemic adverse effect of oral therapy, such as sedation, fatigue, dizziness, and confusion.[5]

References:

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