

What’s New in the Patient Safety World

January 2020

FDA Warning on Gabapentinoids

In the past 2 years we’ve done a couple columns on dangers of gabapentinoids, alone or in combination with opioids (see our What's New in the Patient Safety World columns for November 2017 [“Bad Combination: Gabapentin and Opioids”](#) and March 2019 [“Gabapentin and Pregabalin on the Radar Screen”](#)). So, it comes as no surprise to us that the FDA has just issued a warning about gabapentinoids ([FDA 2019](#)).

The FDA warns that “serious breathing difficulties may occur in patients using gabapentin (Neurontin, Gralise, Horizant) or pregabalin (Lyrica, Lyrica CR) who have respiratory risk factors. These include the use of opioid pain medicines and other drugs that depress the central nervous system, and conditions such as chronic obstructive pulmonary disease (COPD) that reduce lung function. The elderly are also at higher risk.”

The FDA notes that gabapentinoids are often being combined with CNS depressants (including opioids, anti-anxiety medicines, antidepressants, and antihistamines), which increases the risk of respiratory depression. It acknowledges that there is less evidence supporting the risk of serious breathing difficulties in healthy individuals taking gabapentinoids alone.

The FDA decision was based upon both reports it received and studies in the medical literature. Of fatal cases involving gabapentinoids reported to the FDA, all had at least one additional risk factor.

They reviewed results of two randomized, double-blind, placebo-controlled clinical trials in healthy people, three observational studies, and several studies in animals.

The FDA cautions both patients and healthcare professionals that this evidence is “contrary to the widely held belief that gabapentinoids lack drug interactions and have wide therapeutic indices”. It notes that published studies demonstrate these drugs can behave in an additive way to potentiate central nervous system (CNS) and respiratory depression.

Use of gabapentinoids has increased dramatically in recent years. The FDA notes that between 2012 and 2016, the number of patients who filled a gabapentin prescription increased from 8.3 million to 13.1 million annually, and the number of patients who filled a pregabalin prescription increased from 1.9 million to 2.1 million annually. Also, a 2016 office-based physician survey showed that 14 percent and 19 percent of patient encounters involving gabapentin and pregabalin, respectively, also involved opioids.

Gabapentinoids have been important drugs in managing seizure disorders and chronic pain. But they have also been used for a variety of off-label conditions and a recent systematic review of gabapentinoid (pregabalin and gabapentin) abuse ([Evoy 2017](#)) found that increasing numbers of patients are self-administering higher than recommended doses to achieve euphoric highs.

Note that this year's Updated AGS Beers Criteria® for Potentially Inappropriate Medication Use in Older Adults ([AGS 2019](#)) also specifically mentioned the dangers of drug-drug interactions between opioids and gabapentinoids. They noted these drug interactions are problematic in all persons, but are growing increasingly common and may lead to greater harm in vulnerable older adults.

The problems related to gabapentinoids have attracted attention not only in the US, but in other countries as well. Our March 2019 What's New in the Patient Safety World column "[Gabapentin and Pregabalin on the Radar Screen](#)" discussed multiple studies from Australia and Sweden. The Medical Council of Ireland has also recently issued a warning about gabapentinoids ([Medical Council of Ireland 2019](#)). While that warning focused primarily on benzodiazepines and z-drugs, it also called out Pregabalin. A recent population-based study from Sweden ([Molero 2019](#)) suggests that gabapentinoids are associated with an increased risk of suicidal behavior, unintentional overdoses, head/body injuries, and road traffic incidents and offenses. Pregabalin was associated with higher hazards of these outcomes than gabapentin.

In our March 2019 What's New in the Patient Safety World column "[Gabapentin and Pregabalin on the Radar Screen](#)" we cautioned that prescribers need to be aware that concomitant use of pregabalin and opioids or sedating agents may be dangerous and that we need to use our CPOE and e-prescribing systems to alert prescribers when such combinations are in play. But keep in mind that IT interoperability issues may be problematic when drugs are prescribed or dispensed by different healthcare professionals.

Our previous columns on dangers of gabapentinoids alone or in combination with opioids:

- November 2017 [“Bad Combination: Gabapentin and Opioids”](#)
- March 2019 [“Gabapentin and Pregabalin on the Radar Screen”](#)

References:

FDA (US Food and Drug Administration). FDA warns about serious breathing problems with seizure and nerve pain medicines gabapentin (Neurontin, Gralise, Horizant) and pregabalin (Lyrica, Lyrica CR) When used with CNS depressants or in patients with lung problems 12-19-2019

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