Gabapentin and pregabalin – Safety update

- On December 19, 2019, the FDA warned that serious breathing difficulties may occur in patients using gabapentin (Neurontin®, Gralise®, Horizant®) or pregabalin (Lyrica®, Lyrica CR) who have respiratory risk factors.
    - Respiratory risk factors include the use of opioid pain medicines and other drugs that depress the central nervous system (CNS), and conditions such as chronic obstructive pulmonary disease that reduce lung function. The elderly are also at higher risk.
- The FDA evaluation shows that the use of these medicines, often referred to as gabapentinoids, has been growing for prescribed medical use, as well as misuse and abuse.
- Gabapentinoids are FDA-approved to treat a variety of conditions including partial seizures and nerve pain from spinal cord injury, shingles, and diabetes. Other approved uses include fibromyalgia and restless legs syndrome.
- Gabapentinoids are often being combined with CNS depressants, which increases the risk of respiratory depression. CNS depressants include opioids, anti-anxiety medicines, antidepressants, and antihistamines.
- There is less evidence supporting the risk of serious breathing difficulties in healthy individuals taking gabapentinoids alone.
- The FDA reviewed data from the FDA Adverse Event Reporting System (FAERS) database and the medical literature.
    - A search of FAERS from January 1, 2012, to October 26, 2017, identified 49 cases of respiratory depression with gabapentinoids. Ninety-two percent of the cases reported either a respiratory risk factor, including age-related loss of lung function, or the use of a CNS depressant. Twenty-four percent of the cases resulted in death (n = 12).
    - Several small randomized trials of healthy volunteers showed that gabapentinoids alone and in combination with opioids depress respiratory function.
    - Observational studies suggest that patients exposed to preoperative gabapentinoids have an increased risk of postoperative respiratory depression compared to those not exposed to gabapentinoids preoperatively.
- 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 depressant such as a benzodiazepine.
- Patients and caregivers should seek medical attention immediately if they or someone they are caring for experiences symptoms of respiratory problems, because these can be life-threatening. Symptoms to watch for include confusion or disorientation; unusual dizziness or lightheadedness; extreme sleepiness or lethargy; lowed, shallow, or difficult breathing; unresponsiveness; and bluish-colored or tinted skin, especially on the lips, fingers, and toes.
- The FDA is requiring new warnings about the risk of respiratory depression be added to the prescribing information of the gabapentinoids.
- Drug manufacturers are also required to conduct clinical trials to further evaluate their abuse potential, particularly in combination with opioids, because misuse and abuse of these products

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together is increasing, and co-use may increase the risk of respiratory depression. Special attention will be paid to the respiratory depressant effects during this abuse potential evaluation.