OSTEOPOROSIS DRUG INCREASES HYPOCALCEMIA RISK IN DIALYSIS PATIENTS

- The Food and Drug Administration has issued a *Drug Safety Communication* regarding the osteoporosis drug denosumab (Prolia). The communication warns of an increased risk of significant hypocalcemia with denosumab use in patients with advanced kidney disease, especially if they also receive dialysis.
- Nurses and NPs need to assess for hypocalcemia in patients with advanced kidney disease who receive denosumab. Patient education concerning the need for calcium and vitamin D supplements and repeated laboratory monitoring is crucial.

The Food and Drug Administration (FDA) has issued a *Drug Safety Communication* regarding the osteoporosis drug denosumab (Prolia). Interim findings from two studies, an ongoing FDA-required manufacturer's long-term safety study of patients with osteoporosis who take denosumab and a separate internal FDA study evaluating hypocalcemia in dialysis patients receiving denosumab, indicate an increased risk of significant hypocalcemia in those with advanced kidney disease, especially in those who also receive dialysis. Some patients needed hospitalization and some died from the hypocalcemia. While denosumab's labeling has always indicated a risk of hypocalcemia, the new data indicate a more severe risk than previously believed.

Denosumab is a human monoclonal antibody with affinity for receptor activator of nuclear factor kappa-β ligand. Blockage of this receptor inhibits osteoclast formation, function, and survival, preventing the breaking down and resorption of bone. Denosumab is administered by subcutaneous injection once every six months.

Denosumab, originally approved in 2010, is currently approved as a treatment for men and postmenopausal women at high risk for fracture from osteoporosis, and for glucocorticoid-induced osteoporosis in men and women at high risk for fracture. It is also approved to increase bone mass in men at high risk for fracture who are receiving androgen deprivation therapy for nonmetastatic prostate cancer and for women at high risk for fracture who are receiving adjuvant aromatase inhibitor therapy for breast cancer.

Prior to initial administration of denosumab, nurses and NPs should assess the patient's laboratory findings for hypocalcemia, as this must be corrected before starting treatment. Nurses and NPs caring for patients with severe chronic kidney disease, especially those on dialysis, should closely monitor the patient for electrolyte imbalances. In addition to hypocalcemia, patients are at risk for hypophosphatemia, since hypocalcemia triggers the production of parathyroid hormone, which stimulates the kidneys to excrete phosphate. Nurses should educate patients on which dietary choices are rich in calcium and vitamin D and explain why supplements of these nutrients are recommended (the denosumab labeling recommends 1,000 mg of calcium and at least 400 IU of vitamin D daily). Patients should understand the importance of frequent monitoring of blood calcium levels. Nurses should teach patients about the symptoms of hypocalcemia, such as unusual tingling or numbness in the hands, arms, legs, or feet; painful muscle spasms or cramps; laryngospasms or bronchospasms that cause difficulty speaking and breathing; vomiting; seizures; and arrhythmias. Nurses and other health care professionals, as well as patients, can report any adverse effects from denosumab to the FDA MedWatch program at www.accessdata.fda.gov/scripts/medwatch/index.cfm. To read the FDA's *Drug Safety Communication* regarding denosumab, go to www.fda.gov/drugs/drug-safety-and-availability/fda-investigating-risk-severe-hypocalcemia-patients-dialysis-receiving-osteoporosis-medicine-prolia.

ILLICIT DRUGS MAY CONTAIN VETERINARY TRANQUILIZER

- There has been a rise in illicit drugs such as fentanyl being mixed with xylazine, a veterinary tranquilizer. Xylazine is not an opioid; although opioids and xylazine induce similar respiratory symptoms, naloxone will not reverse a xylazine overdose. Severe necrotic skin ulcerations are also possible from frequent exposure to xylazine.
- Nurses who encounter patients with severe necrotic skin ulcerations or respiratory symptoms should consider xylazine overdose and attempt to determine if xylazine abuse is the root cause.

The current opioid crisis has been worsened by the addition of other drugs and substances, including other illicit drugs. There has been a reported rise in the incidence of overdoses from fentanyl, heroin, and other drugs being combined with xylazine, a nonopioid veterinary tranquilizer that is not approved for human use. The drug is added to opioids to purportedly lengthen their euphoric effect. According to the National Institute on Drug Abuse, overdose deaths linked to xylazine started in the eastern United States and spread west, with the largest impact still seen in the Northeast.

Street names for xylazine include tranq, tranq dope, Philly dope, and zombie drug. Xylazine

has a chemical structure similar to clonidine, and like clonidine it acts as a central α_2-adrenergic receptor agonist in the brainstem. This causes a rapid decrease in the release of norepinephrine and dopamine in the central nervous system.

Overdose from xylazine can lead to drowsiness, amnesia, respiratory depression, bradycardia, hypotension, hypothermia, miosis, and elevated blood glucose levels. When xylazine is taken in combination with opioids and other central nervous system depressants (such as alcohol or benzodiazepines), the risk of a fatal overdose is increased. The respiratory symptoms of an opioid overdose and a xylazine overdose are very similar. One problem for emergency health care providers is that because xylazine is not an opioid, it does not respond to naloxone—the antidote for opioid overdose. It is not recommended to use a veterinary medicine (such as yohimbine hydrochloride or tolazoline hydrochloride) for reversing xylazine overdose as it is unknown if these drugs are safe or effective in humans. Another problem for emergency health care providers is that xylazine does not show up on routine toxicology screens, only in specialized toxicology tests.

Repeated use of xylazine or drug combinations with xylazine via injecting, snorting, swallowing, or inhaling can lead to severe necrotic skin ulcerations. These ulcerations look different from typical cellulitis or abscesses and may form in areas of the body that are not the site of the injection. Xylazine dependence occurs from repeated exposure and suddenly stopping the drug will lead to severe withdrawal symptoms.

Nurses who work in EDs should consider xylazine overdose if a patient believed to have overdosed on opioids does not respond to naloxone treatment. Xylazine abuse should also be considered if the patient has unique, severe necrotic skin ulcerations. To assist in tracking the severity of this problem, all adverse effects from possible illicit xylazine exposure should be reported to the FDA's MedWatch program at www.accessdata.fda.gov/scripts/medwatch/index.cfm.

To read the FDA's full warning letter, go to www.fda.gov/media/162981/download.

INCOMPATIBILITY OF SOME PREFILLED GLASS SYRINGES AND LUER-ACTIVATED NEEDLELESS VALVE CONNECTORS

- Some needleless Luer-activated valve connectors with internal pins are not compatible with certain prefilled glass syringes. The internal pin can block the glass syringe tip and prevent drug administration.
- Nurses should be aware of this risk and assist in evaluating the Luer-activated valve connectors used in their organization.

Needleless Luer access devices have been used since the 1990s to prevent needlestick injuries. The Food and Drug Administration (FDA) is warning health care professionals that some prefilled glass syringes will not work properly with Luer-activated valve (LAV) connectors, which have an internal pin mechanism.

A November 2022 FDA alert provides a link to an example of this problem that occurred with prefilled glass syringes of naloxone, reported April 8, 2021, from the Institute for Safe Medication Practices (see www.ismp.org/resources/do-not-use-dr-reddys-prefilled-glass-naloxone-syringes-clavemicroclave-connector). In this example, one hospital discovered that using the prefilled glass syringe of naloxone from Dr. Reddy's Laboratories with a Clave or MicroClave needleless connector caused the pin in the MicroClave LAV access system to break off or clog the glass syringe's tip, preventing the medication from being ejected from the syringe. The article also noted that a similar style LAV connector is made by Bectin Dickinson, B. Braun, and Vygon. (At that time, none of these products had been implicated in an incident involving an incompatible glass syringe.) The new FDA warning does not elaborate on which products have been associated with incompatibilities.

In 2011, the FDA reported incompatibility issues with prefilled glass syringes for adenosine and amiodarone and LAV connectors. Since that time, the agency has been working to finalize guidance for manufacturers to correct this incompatibility problem.

Nurses should be aware that some prefilled glass syringes may not be compatible with the LAV connector used in their organization. These incompatibilities can lead to potentially critical delays in drug administration, since the nurse would need to troubleshoot the problem and come up with a workaround during an emergency. Nurses need to be active on product evaluation committees to help guide their organization to avoid the purchase of equipment incompatible with other products, which can cause a potential safety risk to patients.

For a list of suggestions from the FDA to address this problem, go to www.fda.gov/drugs/drug-safety-and-availability/fda-alerts-health-care-professionals-compatibility-issues-prefilled-glass-syringes-and-certain-luer. To read the FDA alert regarding compatibility issues with prefilled glass syringes and certain LAV connectors, go to www.fda.gov/drugs/drug-safety-and-availability/fda-alerts-health-care-professionals-compatibility-issues-prefilled-glass-syringes-and-certain-luer. ▼

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