Important Drug Safety Notice

TO ALL PARTICIPATING PHARMACIES

Circular Letter MC22-088-CG
November 23, 2022

FDA announced that, is investigating the risk of severe hypocalcemia with serious outcomes, including hospitalization and death, in patients with advanced kidney disease on dialysis treated with the osteoporosis medicine Prolia (denosumab). FDA's review of interim results from an ongoing safety study of Prolia suggests an increased risk of hypocalcemia, or low calcium levels in the blood, in patients with advanced kidney disease. Preliminary results from a separate internal FDA study further investigating hypocalcemia in dialysis patients treated with Prolia show a substantial risk with serious outcomes, including hospitalization and death.

RECOMMENDATIONS

1. Patients

a. Patients should not stop Prolia treatment without first consulting your health care professional, as stopping may worsen your bone condition.

b. Talk to your health care professional about any concerns you may have, including possible alternative treatments.

c. Tell your health care professional if you experience any symptoms of low blood calcium levels such as unusual tingling or numbness in the hands, arms, legs, or feet; painful muscle spasms or cramps; voice box or lung spasms causing difficulty breathing; vomiting; seizures; or irregular heart rhythm.

2. Health Care Professionals

a. Health care professionals should consider the risks of hypocalcemia with the use of Prolia in patients on dialysis.

b. When Prolia is used in these patients, adequate calcium and vitamin D supplementation and frequent blood calcium monitoring, possibly more often than is already being conducted, may help decrease the likelihood or severity of these risks.

c. Advise patients on dialysis to immediately seek help if they experience symptoms of hypocalcemia.

3. Expect patients to visit your pharmacy asking for information on this safety issue and prepare your pharmacy staff on how to handle the situation.

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Prolia (denosumab) by Amgen: Drug Safety Communication - FDA Investigating Risk of Severe Hypocalcemia in Patients on Dialysis

[Posted 11/22/2022]

AUDIENCE: Patient, Health Professional, Pharmacy

ISSUE: The FDA is investigating the risk of severe hypocalcemia with serious outcomes, including hospitalization and death, in patients with advanced kidney disease on dialysis treated with the osteoporosis medicine Prolia (denosumab). FDA's review of interim results from an ongoing safety study of Prolia suggests an increased risk of hypocalcemia, or low calcium levels in the blood, in patients with advanced kidney disease. Preliminary results from a separate internal FDA study further investigating hypocalcemia in dialysis patients treated with Prolia show a substantial risk with serious outcomes, including hospitalization and death.

Because of the frequency and seriousness of these risks, the FDA is alerting health care professionals and patients about them and is continuing to evaluate this potential safety issue with Prolia use in patients with advanced kidney disease, particularly those on dialysis. The FDA will communicate the final conclusions and recommendations when the review is completed and there is more information to share.

BACKGROUND: Prolia is a prescription medicine approved in June 2010 to treat postmenopausal women with osteoporosis at high risk for bone fracture. Prolia was later approved to treat men with osteoporosis, glucocorticoid induced osteoporosis, bone loss in men receiving androgen deprivation therapy for prostate cancer and in women receiving aromatase inhibitor therapy for breast cancer. Prolia works by blocking a protein called RANK (receptor activator of nuclear factor kappa beta) and helps prevent bone cells called osteoclasts from breaking down bone in the body. A health care professional administers Prolia by injection once every six months.

RECOMMENDATIONS:

Patients

- Patients should not stop Prolia treatment without first consulting your health care professional, as stopping may worsen your bone condition.
- Talk to your health care professional about any concerns you may have, including possible alternative treatments.
- Tell your health care professional if you experience any symptoms of low blood calcium levels such as unusual tingling or numbness in the hands, arms, legs, or feet; painful muscle

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spasms or cramps; voice box or lung spasms causing difficulty breathing; vomiting; seizures; or irregular heart rhythm.

Health Care Professionals

- Health care professionals should consider the risks of hypocalcemia with the use of Prolia in patients on dialysis.
- When Prolia is used in these patients, adequate calcium and vitamin D supplementation and frequent blood calcium monitoring, possibly more often than is already being conducted, may help decrease the likelihood or severity of these risks.
- Advise patients on dialysis to immediately seek help if they experience symptoms of hypocalcemia.

Patients and health care professionals are encouraged to report adverse events or side effects related to the use of these products to the FDA's MedWatch Safety Information and Adverse Event Reporting Program:

- Complete and submit the report online.
- Download form or call 1-800-332-1088 to request a reporting form, then complete and return to the address on form, or submit by fax to 1-800-FDA-0178.

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