FDA safety update – Prolia® (denosumab)

- On January 19, 2024, the FDA announced the addition of a *Boxed Warning* to the Prolia (denosumab) drug label regarding the risk of severe hypocalcemia in patients with advanced chronic kidney disease (CKD).

- Prolia is indicated for the treatment of:

    - Postmenopausal women with osteoporosis at high risk for fracture;
    - Increase bone mass in men with osteoporosis;
    - Glucocorticoid-induced osteoporosis;
    - Bone loss in men receiving androgen deprivation therapy for prostate cancer; and
    - Bone loss in women receiving adjuvant aromatase inhibitor therapy for breast cancer

- Based on a completed FDA review of available information, the FDA has concluded that Prolia increases the risk of severe hypocalcemia in patients with advanced CKD, particularly patients on dialysis.

- Severe hypocalcemia appears to be more common in patients with CKD who also have a condition known as mineral and bone disorder (CKD-MBD). In patients with advanced CKD taking Prolia, severe hypocalcemia resulted in serious harm, including hospitalization, life-threatening events, and death.

- Severe hypocalcemia can be asymptomatic or may present with symptoms that include confusion; seizures; irregular heart rhythm; fainting; face twitching; uncontrolled muscle spasms; or weakness, tingling, or numbness in parts of the body.

- Patients already on Prolia should discuss calcium and vitamin D intake, appropriate laboratory monitoring, risk for hypocalcemia, and any other issues that may be related to their Prolia therapy. Patients should not stop taking Prolia without talking with their health care provider as the risk of bone fracture is increased when therapy is stopped, skipped or delayed.

- Healthcare providers should evaluate the appropriateness of Prolia in patients with advanced CKD. Treatment of these patients, including those on dialysis, and particularly patients with diagnosed CKD-MBD should involve a health care provider with expertise in the diagnosis and management of CKD-MBD.

- Proper management of CKD-MBD, correction of hypocalcemia, and supplementation with calcium and activated vitamin D prior to Prolia treatment is expected to decrease the risk of developing severe hypocalcemia and any associated complications.

- Following Prolia administration, close monitoring of blood calcium levels and prompt management of hypocalcemia is essential to prevent complications such as seizures or arrhythmias. Advise patients to promptly report symptoms that could be consistent with hypocalcemia.