



PROLIA[®] REMS

FDA Required REMS Safety Information

Serious Risks Associated with Prolia[®] (denosumab)

- Hypocalcemia
- Osteonecrosis of the Jaw
- Atypical Femoral Fractures
- Serious Infections
- Dermatologic Reactions

May 2015

Important Safety Update

Dear Healthcare Provider:

The FDA has required this safety update as part of the PROLIA[®] REMS (**R**isk **E**valuation and **M**itigation **S**trategy) to inform healthcare providers about the following **serious risks of Prolia[®]**:

Hypocalcemia

- Hypocalcemia may be exacerbated by the use of Prolia[®].

Osteonecrosis of the Jaw

- Osteonecrosis of the jaw (ONJ) has been reported in patients receiving Prolia[®].

Atypical Subtrochanteric and Diaphyseal Femoral Fractures

- Atypical low-energy or low trauma subtrochanteric and diaphyseal femoral fractures, which may be bilateral, have been reported in patients receiving Prolia[®]. Atypical femoral fractures most commonly occur with minimal or no trauma to the affected area.

Serious Infections

- In a clinical trial, women with postmenopausal osteoporosis treated with Prolia[®] presented with serious infections, such as serious skin infection and endocarditis, leading to hospitalization more frequently than the placebo group.

Dermatologic Reactions

- In a clinical trial, women with postmenopausal osteoporosis treated with Prolia[®] presented with generalized epidermal and dermal adverse events at a significantly higher rate compared to the placebo group. These included dermatitis, eczema, and rashes.

Role of the Healthcare Provider

- ✓ **Make note** of these risks and discuss them with your patients using the non-promotional **Patient Counseling Toolkit**, which includes:
 - **Patient Counseling Chart for Healthcare Providers**
 - **Patient Brochure**
 - **Prescribing Information**
 - **Medication Guide**
- Note: these materials are available to order through 1-800-77-AMGEN (1-800-772-6436), by downloading the information from www.proliahcp.com/risk-evaluation-mitigation-strategy, or by contacting your local Amgen Sales Representative.
- ✓ **Review** information in the **Medication Guide and Patient Counseling Chart** with your patients, including the serious risks of Prolia[®] and the symptoms of each risk.
- ✓ **Advise** each patient to seek prompt medical attention if they have signs or symptoms of any of the serious risks.
- ✓ **Provide** each patient a copy of the **Medication Guide** and **Patient Brochure**.
- ✓ **Visit** www.proliahcp.com/risk-evaluation-mitigation-strategy for more information about the Prolia[®] REMS.

Indication

Prolia[®] is a RANK ligand (RANKL) inhibitor indicated for the:

- 1) treatment of postmenopausal women with osteoporosis at high risk for fracture,
- 2) treatment to increase bone mass in men with osteoporosis at high risk for fracture,
- 3) treatment to increase bone mass in men at high risk for fracture receiving androgen deprivation therapy for nonmetastatic prostate cancer, and
- 4) treatment to increase bone mass in women at high risk for fracture receiving adjuvant aromatase inhibitor therapy for breast cancer

This letter does not contain the complete safety profile for Prolia[®]. Please review the Prescribing Information and Medication Guide, enclosed.

Reporting Adverse Events

You are encouraged to report negative side effects of prescription drugs to the FDA. Visit www.fda.gov/medwatch, or call 1-800-FDA-1088. Healthcare providers should report all suspected adverse events associated with Prolia[®] to the FDA or to Amgen at 1-800-772-6436.

Sincerely,



Isma Benattia, MD
Vice President, Global Patient Safety
Amgen

[Attachment of the Prolia[®] Prescribing Information and Medication Guide]