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**Initial REMS Approval: 06/01/10**

**Most Recent Modification: 05/2015**

## **BL 125320 PROLIA<sup>®</sup> (denosumab)**

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### **RISK EVALUATION AND MITIGATION STRATEGY (REMS)**

#### **1. Goals**

The goal of the PROLIA<sup>®</sup> REMS is to mitigate the risks of hypocalcemia, osteonecrosis of the jaw, atypical femoral fractures, serious infections, and dermatologic reactions by:

- a. informing healthcare providers and patients about the risks of (1) hypocalcemia, (2) osteonecrosis of the jaw, (3) atypical femoral fractures, (4) serious infections, and (5) dermatologic reactions associated with PROLIA<sup>®</sup>
- b. informing healthcare providers they should counsel patients about the risks associated with PROLIA<sup>®</sup>.

#### **2. REMS Elements**

##### **2.1 Medication Guide**

Amgen will ensure the PROLIA<sup>®</sup> Medication Guide is distributed in accordance with 21 CFR 208.24.

The [Medication Guide](#) is part of the REMS and is appended.

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## 2.2 Communication Plan

Amgen will implement the following communication plan to healthcare providers likely to prescribe PROLIA<sup>®</sup>. The communication plan will include:

### 2.2.1 REMS Letters

Amgen will send a [REMS Letter for Healthcare Providers](#) and [REMS Letter for Professional Societies](#) within 60 calendar days of this REMS modification and again 1 year after approval of this REMS modification. The REMS Letters will address potential risks of (1) hypocalcemia, (2) osteonecrosis of the jaw, (3) atypical femoral fractures, (4) serious infections, and (5) dermatologic reactions associated with PROLIA<sup>®</sup>.

The [REMS Letter for Healthcare Providers](#) will be distributed by US mail. If the [REMS Letter for Healthcare Providers](#) is undeliverable, Amgen will use available resources to obtain updated address information and send a second letter via US mail within 45 calendar days of return. If the correct address cannot be obtained, the attempt will be documented and no further communication will occur.

The [REMS Letter for Professional Societies](#) will be sent as an attachment to an email. If the email is undeliverable or marked as unopened, a second email will be sent within 7 calendar days. If the second email is undeliverable or marked as unopened, the REMS letter will be mailed within 30 calendar days.

A copy of, or a link to, the Prescribing Information (PI) and [Medication Guide](#) will accompany each REMS Letter.

### REMS Letter for Healthcare Providers

The intended audience for the [REMS Letter for Healthcare Providers](#) will be endocrinologists, rheumatologists, obstetricians/gynecologists, primary care physicians, oncologists, and urologists.

The [REMS Letter for Healthcare Providers](#) will also be available via a link from the [PROLIA<sup>®</sup> REMS website](#), through Amgen's Medical Information Department, and from Amgen's sales and/or medical representatives upon request for one year after the approval of this REMS modification (05/2015).

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## **REMS Letter for Professional Societies**

Amgen will send the [REMS Letter for Professional Societies](#) to the following professional societies and organizations requesting the letter or its content be provided to their membership.

- National Osteoporosis Foundation
- American Society of Bone Mineral Research
- American College of Rheumatology
- American Association of Clinical Endocrinologists
- American Academy of Family Physicians
- Endocrine Society
- American Society of Clinical Oncology
- North American Menopause Society

### **2.2.2. Patient Counseling Toolkit**

Amgen will provide healthcare providers with a Patient Counseling Toolkit, including a [Patient Counseling Chart for Healthcare Providers](#), a [Patient Brochure](#), and copies of the PI and [Medication Guide](#). Throughout the duration of the REMS, the contents of the Patient Counseling Toolkit will be detailed to targeted healthcare providers (eg, endocrinologists, rheumatologists, obstetricians/gynecologists, primary care physicians, oncologists, urologists) where Amgen has sales representatives deployed to speak with healthcare providers in the field. These targeted healthcare providers include prescribers who are likely to prescribe PROLIA<sup>®</sup>.

### **Patient Counseling Chart for Healthcare Providers**

Amgen will provide a [Patient Counseling Chart for Healthcare Providers](#), which will be a standalone tool for healthcare providers to counsel patients. Amgen sales or medical representatives will verbally discuss the risk messages contained in the [Patient Counseling Chart for Healthcare Providers](#) during the visit with the healthcare provider.

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## **Patient Brochure**

The [Patient Brochure](#) includes information on risk messages and will be provided to healthcare provider offices as an additional counseling tool for patients.

### **2.2.3. Journal Information Piece**

Amgen will publish a [journal information piece](#) quarterly for 12 months after approval of the REMS modification (05/2015) in the following professional journals:

- Journal of the American Medical Association
- Arthritis and Rheumatology
- Endocrine Today

### **2.2.4. Dissemination of REMS Information at Scientific Meetings**

The PROLIA<sup>®</sup> REMS Patient Counseling Toolkit will be prominently displayed at relevant scientific meetings where Amgen has a PROLIA<sup>®</sup> commercial booth presence for the duration of the REMS.

### **2.2.5. REMS Website**

The [PROLIA<sup>®</sup> REMS website](#) for healthcare professionals ([www.proliahcp.com/risk-evaluation-mitigation-strategy](http://www.proliahcp.com/risk-evaluation-mitigation-strategy)) will continue for the duration of the REMS. The REMS website will include the option to print versions of the PI, [Medication Guide](#), [REMS Letter for Healthcare Providers](#), [Patient Counseling Chart for Healthcare Providers](#), [Patient Brochure](#), and [journal information piece](#). The PROLIA<sup>®</sup> product website will include a prominent REMS-specific link to [PROLIA<sup>®</sup> REMS website](#). All website information will be updated within 60 days post approval of the modification.

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The following are part of the PROLIA<sup>®</sup> REMS and are appended:

- [REMS Letter for Healthcare Providers](#)
- [REMS Letter for Professional Societies](#)
- [Patient Counseling Chart for Healthcare Providers](#)
- [Patient Brochure](#)
- [Journal Information Piece](#)
- [REMS Website \(landing page\)](#)

### **3. Timetable for Submission of Assessments**

Amgen will submit REMS Assessments to FDA at 18 months, 3, 6, and 7 years from the date of the initial approval (01 June 2010) of the REMS. To facilitate inclusion of as much information as possible while allowing reasonable time to prepare the submission, the reporting interval covered by each assessment will conclude no earlier than 60 days before the submission date for that assessment. Amgen will submit each assessment so that it will be received by the FDA on or before the due date.