

## ROUTING FORM

First Mechanical ☐

Final Mechanical ☐

Job #: \_\_\_\_\_

☐ Patient Facing Materials  
(requires Euro Legal Review)

Client: \_\_\_\_\_ Product: \_\_\_\_\_

Description: \_\_\_\_\_

☐ Client Comments Received/Transcribed Date: \_\_\_\_\_ Initials: \_\_\_\_\_

Operator: \_\_\_\_\_ Extension: \_\_\_\_\_ Date: \_\_\_\_\_ Time: \_\_\_\_\_

PM: \_\_\_\_\_ Extension: \_\_\_\_\_ ArtDir: \_\_\_\_\_ Extension: \_\_\_\_\_

### SIGN-OFF

### INITIALS

### DATE

### TIME

### COMMENTS

Art Director

**REVISED**

☐ OK ☐ Corrections

Art Supervisor

1:41 pm, Dec 23, 2020

☐ OK ☐ Corrections

Editor

☐ OK ☐ Corrections

Editor 2—Double Read ☐

☐ OK ☐ Corrections

Copywriter

☐ OK ☐ Corrections

Copy Supervisor

☐ OK ☐ Corrections

Creative Director Art

☐ OK ☐ Corrections

Creative Director Copy

☐ OK ☐ Corrections

Assoc. Creative Director

☐ OK ☐ Corrections

Account Executive

☐ OK ☐ Corrections

Account Supervisor

☐ OK ☐ Corrections

Acct. Group Supervisor

☐ OK ☐ Corrections

Sr. Mgmt. Supervisor

☐ OK ☐ Corrections

Medical Director

☐ OK ☐ Corrections

Production

☐ OK ☐ Corrections

Art Buyer

☐ OK ☐ Corrections

### NOTES



1. Study of Persistence Among Osteoporosis Treatments at 3 Years
2. Study of Persistence Among Osteoporosis Treatment at 3 Years
3. Study of Prolia® (denosumab)
4. 3-Year Persistence Study of PMO Treatments
5. Persistence Data of PMO Treatment at 3 Years
6. Persistence Study of PMO Treatments
7. 3-Year Persistence Study of Postmenopausal Osteoporosis Treatments
8. Persistence Data of Postmenopausal Osteoporosis Treatment at 3 Years
9. Persistence Study of Postmenopausal Osteoporosis Treatments

**Contraindications:** Prolia<sup>®</sup> is contraindicated in patients with hypocalcemia. Pre-existing hypocalcemia must be corrected prior to initiating Prolia<sup>®</sup>. Prolia<sup>®</sup> is contraindicated in women who are pregnant and may cause fetal harm. In women of reproductive potential, pregnancy testing should be performed prior to initiating treatment with Prolia<sup>®</sup>. Prolia<sup>®</sup> is contraindicated in patients with a history of systemic hypersensitivity to any component of the product. Reactions have included anaphylaxis, facial swelling and urticaria.

**Hypersensitivity:** Clinically significant hypersensitivity including anaphylaxis has been reported with Prolia®. Symptoms have included hypotension, dyspnea, throat tightness, facial and upper airway edema, pruritus and urticaria. If an anaphylactic or other clinically significant allergic reaction occurs, initiate appropriate therapy and discontinue further use of Prolia®.

**Osteonecrosis of the Jaw (ONJ):** ONJ, which can occur spontaneously, is generally associated with tooth extraction and/or local infection with delayed healing, and has been reported in patients receiving Prolia®. An oral exam should be performed by the prescriber prior to initiation of Prolia®. A dental examination with appropriate preventive dentistry is recommended for all patients. In patients with risk factors for ONJ such as invasive dental procedures, diagnosis of cancer, concomitant therapies (e.g. chemotherapy, corticosteroids, angiogenesis inhibitors), poor oral hygiene, and co-morbid disorders. Good oral hygiene practices should be maintained during treatment with Prolia®. The risk of ONJ may increase with duration of exposure to Prolia®.

**Atypical Femoral Fractures:** Atypical low-energy, or low trauma fractures of the shaft have been reported in patients receiving Prolia®. Causality has not been established as these fractures also occur in osteoporotic patients who have not been treated with antiresorptive agents.

**Multiple Vertebral Fractures (MVF) Following Discontinuation of Prolia® Treatment:** Following discontinuation of Prolia® treatment, fracture risk increases, including the risk of multiple vertebral fractures. New vertebral fractures occurred as early as 7 months (on average 19 months) after the last dose of Prolia®. Prior vertebral fracture was a predictor of multiple vertebral fractures after Prolia® discontinuation. Evaluate an individual's benefit/risk before initiating treatment with Prolia®. If Prolia® treatment is discontinued, patients should be transitioned to an alternative antiresorptive therapy.

Endocarditis was also reported more frequently in Prolia®-treated patients. The incidence of opportunistic infections and the overall incidence of infections were similar between the treatment groups. Advise patients to seek prompt medical attention if they develop signs or symptoms of severe infection, including cellulitis.

Patients on concomitant immunosuppressant agents or with impaired immune systems may be at increased risk for serious infections. In patients who develop serious infections while on Prolia®, prescribers should assess the need for continued Prolia® therapy.

**Dermatologic Adverse Reactions:** Epidermal and dermal adverse events such as dermatitis, eczema and rashes occurred at a significantly higher rate with Prolia® compared to placebo. Most of these events were not specific to the injection site. Consider discontinuing Prolia® if severe symptoms develop.

**Musculoskeletal Pain:** Severe and occasionally incapacitating bone, joint, and/or muscle pain has been reported in patients taking Prolia®. Consider discontinuing use if severe symptoms develop.

**Suppression of Bone Turnover:** Prolia® resulted in significant suppression of bone remodeling as evidenced by markers of bone turnover and bone histomorphometry. The significance of these findings and the effect of long-term treatment are unknown. Monitor patients for consequences, including ONJ, atypical fractures, and delayed fracture healing.

**Adverse Reactions:** The most common adverse reactions (>5% and more common than placebo) are back pain, pain in extremity, musculoskeletal pain, hypercholesterolemia, and cystitis. Pancreatitis has been reported with Prolia®.

**Reference:** 1. Data on file, Amgen; 2020.

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- A VARIABLE SUBJECT LINE OPTION:**
1. Study of Persistence Among Osteoporosis Treatments at 3 Years
  2. Study of Persistence Among Osteoporosis Treatment at 3 Years
  3. Study of Prolia® (denosumab)
  4. 3-Year Persistence Study of PMO Treatments
  5. Persistence Data of PMO Treatment at 3 Years
  6. Persistence Study of PMO Treatments
  7. 3-Year Persistence Study of Postmenopausal Osteoporosis Treatments
  8. Persistence Data of Postmenopausal Osteoporosis Treatment at 3 Years
  9. Persistence Study of Postmenopausal Osteoporosis Treatments

LTE

8:45 AM

100%

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>

✓

From: [Managed Healthcare Executive]

To: [Insert Customer Email]

Cc:

Persistency Data for 3 Years

Yesterday at 6:25 PM

Message below is a paid advertisement. Content is provided by the sponsor.

Managed Healthcare®

EXECUTIVE

The following promotional message is brought to you by Amgen, which is based on an analysis done by Amgen.

Persistence with Prolia® (denosumab) in postmenopausal osteoporosis patients was higher versus both IV and oral bisphosphonates at 3 years¹

prolia®

(denosumab)injection

INDICATION

Prolia® is indicated for the treatment of postmenopausal women with osteoporosis at high risk for fracture, defined as a history of osteoporotic fracture, or multiple risk factors for fracture; or patients who have failed or are intolerant to other available osteoporosis therapy. In postmenopausal women with osteoporosis, Prolia® reduces the incidence of vertebral, nonvertebral, and hip fractures.

CONTRAINDICATIONS

Prolia® is contraindicated in patients with hypocalcemia, women who are pregnant, and patients with a history of systemic hypersensitivity to any component of the product. Perform pregnancy testing in women of reproductive potential prior to initiating treatment with Prolia®.

Please scroll below for additional Important Safety Information.

Dear [Insert Customer Name],

A study of persistence rates with osteoporosis treatments among women 66 years or older with postmenopausal osteoporosis (PMO) showed that Medicare beneficiaries receiving Prolia® had higher rates of persistence at three years than those on other osteoporosis treatments.¹

PERSISTENCE\* RATES AT 36 MONTHS¹,²

Patients Remaining Persistent on Treatment

40

35

30

25

20

15

10

5

0

Prolia®  
[n = 25,107]

Oral BP  
[n = 79,710]

IV BP  
[n = 179,454]

38%

17%

6%

Active Ingredients

Oral BP:  
77.9% alendronate,  
9.9% risedronate,  
12.3%ibandronate (oral)

IV BP:  
99.4% zoledronate,  
5.6%ibandronate (IV)

BP=bisphosphonates; IV=intravenous.

¹Persistence was defined as the duration of continuous use of a medication from initiation³ to discontinuation. Medication discontinuation was defined as a medication switch or a treatment gap of 60 days or longer. Discontinuation date was defined as the switch date or the last dosing date plus the allowable treatment gap (59 days), whichever is earlier.

²The model was adjusted for patient characteristics, including demographics, health history, number of medications used, previous fracture, and previous osteoporosis medication use.

³Initiation of a medication was defined as no use of medication for at least 1 year before this use (at least 14 months for IV zoledronic acid).

Medicare beneficiaries receiving Prolia® had higher rates of persistence at three years than those on other osteoporosis treatments¹

#### Study Design¹

- The study was conducted to provide 3-year persistence rates of osteoporosis treatments among elderly female Medicare beneficiaries in the US
- This was a retrospective observational study of Medicare beneficiaries who initiated an osteoporosis medication between 2011 and 2014
- Participants were women ≥ 66 years of age at treatment initiation
- The following analyses were done:
  - Percentage of patients in each persistence group (< 12 months, 12 to < 24 months, 24 to < 36 months, and ≥ 36 months) by osteoporosis medication category and patient characteristics in each persistence group
  - Status at the end of persistence (stopped, switched, died, disenrolled from Medicare, end of study) by osteoporosis medication category and persistence group
    - The analyses above were repeated for patients who could be followed for 3 years
  - The association of osteoporosis medication characteristics with persistence adjusted for patient characteristics

#### Study Assumptions and Limitations¹

- Persistence was measured from initiation to discontinuation with an allowable gap of 60 days
- It is not known if patients used the medication—only that the medication was filled
- Results may not generalize to younger patients
- Information bias and unmeasured confounders may exist

Please visit [proliapayerresources.com](http://proliapayerresources.com) for more information about how Prolia® helps protect your members and your plan from costly fractures

### IMPORTANT SAFETY INFORMATION

**Contraindications:** Prolia® is contraindicated in patients with hypocalcemia. Pre-existing hypocalcemia must be corrected prior to initiating Prolia®. Prolia® is contraindicated in women who are pregnant and may cause fetal harm. In women of reproductive potential, pregnancy testing should be performed prior to initiating treatment with Prolia®. Prolia® is contraindicated in patients with a history of systemic hypersensitivity to any component of the product. Reactions have included anaphylaxis, facial swelling and urticaria.

**Same Active Ingredient:** Prolia® contains the same active ingredient (denosumab) found in XGEVA®. Patients receiving Prolia® should not receive XGEVA®.

**Hypersensitivity:** Clinically significant hypersensitivity including anaphylaxis has been reported with Prolia®. Symptoms have included hypotension, dyspnea, throat tightness, facial and upper airway edema, pruritus and urticaria. If an anaphylactic or other clinically significant allergic reaction occurs, initiate appropriate therapy and discontinue further use of Prolia®.

**Hypocalcemia:** Hypocalcemia may worsen with the use of Prolia®, especially in patients with severe renal impairment. In patients predisposed to hypocalcemia and disturbances of mineral metabolism, including treatment with other calcium-lowering drugs, clinical monitoring of calcium and mineral levels is highly recommended within 14 days of Prolia® injection. Concomitant use of calcimimetic drugs may worsen hypocalcemia risk and serum calcium should be closely monitored. Adequately supplement all patients with calcium and vitamin D.

**Osteonecrosis of the Jaw (ONJ):** ONJ, which can occur spontaneously, is generally associated with tooth extraction and/or local infection with delayed healing, and has been reported in patients receiving Prolia®. An oral exam should be performed by the prescriber prior to initiation of Prolia®. A dental examination with appropriate preventive dentistry is recommended prior to treatment in patients with risk factors for ONJ such as invasive dental procedures, diagnosis of cancer, concomitant therapies (e.g. chemotherapy, corticosteroids, angiogenesis inhibitors), poor oral hygiene, and co-morbid disorders. Good oral hygiene practices should be maintained during treatment with Prolia®. The risk of ONJ may increase with duration of exposure to Prolia®.

For patients requiring invasive dental procedures, clinical judgment should guide the management plan of each patient. Patients who are suspected of having or who develop ONJ should receive care by a dentist or an oral surgeon. Extensive dental surgery to treat ONJ may exacerbate the condition. Discontinuation of Prolia® should be considered based on individual benefit-risk assessment.

**Atypical Femoral Fractures:** Atypical low-energy, or low trauma fractures of the shaft have been reported in patients receiving Prolia®. Causality has not been established as these fractures also occur in osteoporotic patients who have not been treated with antiresorptive agents.

During Prolia® treatment, patients should be advised to report new or unusual thigh, hip, or groin pain. Any patient who presents with thigh or groin pain should be evaluated to rule out an incomplete femur fracture. Interruption of Prolia® therapy should be considered, pending a risk/benefit assessment, on an individual basis.

**Multiple Vertebral Fractures (MVF) Following Discontinuation of Prolia® Treatment:** Following discontinuation of Prolia® treatment, fracture risk increases, including the risk of multiple vertebral fractures. New vertebral fractures occurred as early as 7 months (on average 19 months) after the last dose of Prolia®. Prior vertebral fracture was a predictor of multiple vertebral fractures after Prolia® discontinuation. Evaluate an individual's benefit/risk before initiating treatment with Prolia®. If Prolia® treatment is discontinued, patients should be transitioned to an alternative antiresorptive therapy.

**Serious Infections:** In a clinical trial (N = 7808), serious infections leading to hospitalization were reported more frequently in the Prolia® group than in the placebo group. Serious skin infections, as well as infections of the abdomen, urinary tract and ear, were more frequent in patients treated with Prolia®.

Endocarditis was also reported more frequently in Prolia®-treated patients. The incidence of opportunistic infections and the overall incidence of infections were similar between the treatment groups. Advise patients to seek prompt medical attention if they develop signs or symptoms of severe infection, including cellulitis.

Patients on concomitant immunosuppressant agents or with impaired immune systems may be at increased risk for serious infections. In patients who develop serious infections while on Prolia®, prescribers should assess the need for continued Prolia® therapy.

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**Adverse Reactions:** The most common adverse reactions (>5% and more common than placebo) are back pain, pain in extremity, musculoskeletal pain, hypercholesterolemia, and cystitis. Pancreatitis has been reported with Prolia®.

The overall incidence of new malignancies was 4.3% in the placebo group and 4.8% in the Prolia® group. A causal relationship to drug exposure has not been established. Denosumab is a human monoclonal antibody. As with all therapeutic proteins, there is potential for immunogenicity.

**Please see Prolia® full Prescribing Information, including Medication Guide.**

**Reference:** 1. Data on file. Amgen; 2020.

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