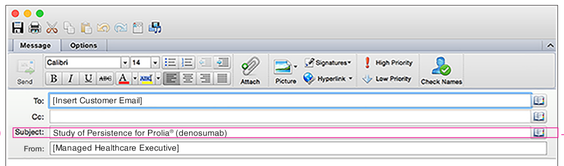
Email 4-DESKTOP



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VARIABLE SUBJECT LINE OPTION:
1. Persistency Data for 3 Years
2. Study of Persistence Among Osteoporosis Treatments at 3 Years
3. Prolia® Persistency Data for 3 Years

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.

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

DOF OP Long-Term Persistence Study: 1/A/Figure

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. 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.

Please scroll below for additional Important Safety Information.

Dear [Insert Customer Name],

A study of persistence rates with osteoporosis treatments among women with postmenopausal osteoporosis (PMO) showed that Medicare beneficiaries receiving Prolia® had higher rates of persistence than those on other osteoporosis treatments at 3 years.

DOF OP Long-Term Persistence Study: 1/A/Figure 1/A/Sec 3.1

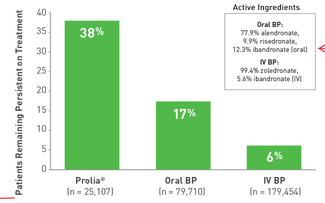
DOF OP Long-Term Persistence Study: 1/A/Figure

DOF OP Long-Term Persistence Study: 1/A/Figure footnotes

DOF OP Long-Term Persistence Study: 3/A/6

DOF OP Long-Term Persistence Study: 1/A/Figure footnotes, 2/A/8

PERSISTENCE* RATES AT 36 MONTHS†



BP=bisphosphonates; IV=intravenous.
*Persistence was defined as the duration of continuous use of a medication from initiation[1] to discontinuation.[1]
†The model was adjusted for patient characteristics, including demographics, health history, number of medications used, previous fracture, and previous osteoporosis medication use.
‡Initiation 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).
§Discontinuation date defined as the switch date or the last dosing date plus the allowable treatment gap (60 days), whichever was earlier.

DOF OP Long-Term Persistence Study: 1/A/Figure footnotes

DOF OP Long-Term Persistence Study: 3/A/Table 1

Medicare beneficiaries receiving Prolia® had higher rates of persistence than those on other osteoporosis treatments at 36 months

DOF OP Long-Term Persistence Study: 2/A/1

Medication categories were denosumab, oral bisphosphonates, IV bisphosphonates, and other medications.

Study Design

- 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

DOF OP Long-Term Persistence Study: 1/A/Sec 4.5

DOF OP Long-Term Persistence Study: 3/A/3

DOF OP Long-Term Persistence Study: 3/A/4

DOF OP Long-Term Persistence Study: 3/A/5

DOF OP Long-Term Persistence Study: 3/A/6

Study Assumptions and Limitations

- 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

DOF OP Long-Term Persistence Study: 4/A/1

DOF OP Long-Term Persistence Study: 4/A/2

Please visit proliapayerresources.com for more information about how Prolia® helps protect your members and your plan from costly fractures

Links to: proliapayerresources.com

IMPORTANT SAFETY INFORMATION

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.

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®.

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.

Links to: http://www.pi.amgen.com/united_states/prolia/prolia_pi.pdf

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

Links to: https://www.pi.amgen.com/~/media/amgen/repositorysites/pi-amgen-com/prolia/prolia_mg.pdf

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

MOBILE

A VARIABLE SUBJECT LINE OPTION:
1. Persistency Data for 3 Years
2. Study of Persistence Among Osteoporosis Treatments at 3 Years
3. Prolia® Persistency Data for 3 Years

LTE 8:45 AM 100%

From: [Managed Healthcare Executive]

To: [Insert Customer Email]

Cc:

Study of Persistence for Prolia® (denosumab) A

Yesterday at 6:25 PM

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Managed Healthcare® EXECUTIVE

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prolia® (denosumab) injection

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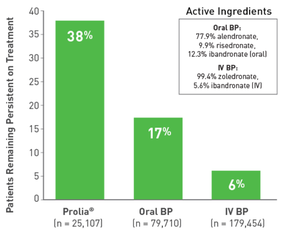

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Please see Prolia® full Prescribing Information, including Medication Guide.

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

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USA-162-82567 11/20