# Email 2- DESKTOP

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To: [Insert Customer Email]

Cc:

Subject: Head-to-head Bone Mineral Density Study With Prolia® vs Alendronate

From: [Managed Healthcare Executive; edigest@email.managedhealthcareexecutive.com]

A

VARIABLE SUBJECT LINE OPTIONS:
1. [Bone Mineral Density Results for Prolia® vs Alendronate]
2. [Bone Mineral Density Results in Head-to-head Study of Prolia® vs Alendronate]
3. [Alendronate vs Prolia®: Bone Mineral Density Results in Women With Postmenopausal Osteoporosis]

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Managed Healthcare EXECUTIVE

The following promotional message is brought to you by Amgen.

## Learn more about a head-to-head bone mineral density (BMD) study comparing alendronate continuation to Prolia® in women with postmenopausal osteoporosis (PMO)

prolia® (denosumab) Injection

### INDICATION

Prolia® (denosumab) 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],

Data used in USA-162-82078, Page 21

Cummings NEJM 2009: 762/B/4; Prolia PI v20: 22/A/3, 22/A/5, 23/A/1; Bone Lancet Diabetes Endocrinol 2017: 2/A/3

### FREEDOM: Pivotal Phase 3 Fracture Trial

During the pivotal Phase 3 fracture trial in postmenopausal women with osteoporosis, Prolia® significantly reduced the relative risk of fracture at 3 years in vertebral, hip, and nonvertebral sites vs placebo.[1-3] Prolia® significantly increased bone mineral density at key sites at 3 years.[1,2]

Links to Prolia HCP website: https://www.proliahcp.com/clinical-studies/safety-efficacy

Review 3-Year Pivotal FREEDOM Study

Data used in USA-162-82078, Page 22

Cummings NEJM 2009: 761/A/2, 761/B/1; Prolia PI v20 03/20: 23/A/2

Data used in USA-162-82078, Page 25; USA-162-81547, Pages 56, 58

Cummings NEJM 2009: 762/A/Table 3; Bone Lancet Diabetes Endocrinol 2017: 5/A/Table 2, 9/A/3

There were no significant differences between subjects who received Prolia® and those who received placebo in the total incidence of adverse events, serious adverse events, or the discontinuation of study treatment because of adverse events. The efficacy and safety of Prolia® in female patients with PMO were further evaluated in a 7-year open-label extension study.[3]

Review 10-year Open-label Extension Study

Data used in USA-162-82078, Page 25

Bone Lancet Diabetes Endocrinol 2017: 2/A/2

Links to Prolia HCP website: https://www.proliahcp.com/clinical-studies/safety-efficacy

### STAND: Prolia® vs Alendronate

A head-to-head BMD study evaluated women with PMO continuing on alendronate or transitioning to Prolia® in a 1-year, multicenter, international, randomized, double-blind, double-dummy, parallel-group Phase 3 trial[4]

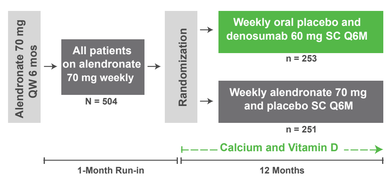
Data used in USA-162-82078, Page 30

Kendler J Bone Miner Res 2010: 73/A/2, 73/A/3

Data used in USA-162-82078, Page 32

Kendler J Bone Miner Res 2010: 76/B/3, 77/A/1

PATIENTS CONTINUING ON ALENDRONATE THERAPY OR TRANSITIONING TO PROLIA® WERE EVALUATED[4]




Q6M=once every 6 months; QW=once a week; SC=subcutaneous.
Primary Endpoint: Percentage change in total hip BMD from baseline to month 12.
Select Secondary Endpoint: Percentage change in BMD at lumbar spine at month 12.
Study Population: Postmenopausal women with a BMD T-score of ≤ -2.0 and ≥ -4.0 at the lumbar spine or total hip. Women must have been receiving alendronate 70 mg/week for ≥ 6 months prior to screening.

Data used in USA-162-82078, Page 29

Kendler J Bone Miner Res 2010: 73/A/2, 73/A/3, 73/B/1, 75/A/Figure 1

Data used in USA-162-82078, Page 30

Kendler J Bone Miner Res 2010: 73/B/3

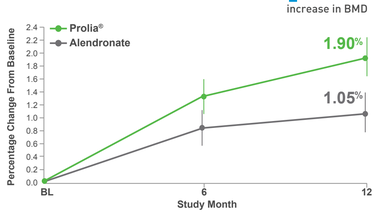
Data used in USA-162-82078, Page 30

Kendler J Bone Miner Res 2010: 73/A/2

Data used in USA-162-82078, Page 31

Kendler J Bone Miner Res 2010: 74/B/4

PROLIA® DEMONSTRATED NONINFERIORITY AND SUPERIORITY (VS ALENDRONATE) IN TOTAL HIP BMD[4]




The lower limit of the confidence interval excluded the prespecified noninferiority margin (-0.35% for total hip), thus showing the noninferiority of Prolia® compared with alendronate.
Superiority testing demonstrated that the BMD increase with denosumab at the total hip was statistically superior to the change with alendronate ($P < 0.0001$).
*95% CI 0.44%-1.25%, $P < 0.01$.

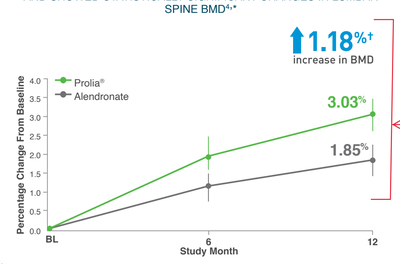
Data used in USA-162-82078, Page 31

Kendler J Bone Miner Res 2010: 74/B/4, 76/A/Figure 2

Data used in USA-162-82078, Page 31

Kendler J Bone Miner Res 2010: 74/B/4

PROLIA® DEMONSTRATED NONINFERIORITY (VS ALENDRONATE) AND SHOWED STATISTICALLY SIGNIFICANT CHANGES IN LUMBAR SPINE BMD[4,*]




The lower limit of the confidence interval excluded the prespecified noninferiority margin (-0.22% for lumbar spine), thus showing the noninferiority of Prolia® compared with alendronate.
*Secondary endpoint.
†95% CI 0.63%-1.73%, $P < 0.01$.

Data used in USA-162-82078, Page 31

Kendler J Bone Miner Res 2010: 74/B/5

Data used in USA-162-82078, Page 31

Kendler J Bone Miner Res 2010: 74/B/5, 76/A/Figure 2

Data used in USA-162-82078, Page 31

Kendler J Bone Miner Res 2010: 73/B/3

BMD data results are not meant to imply fracture efficacy and should not be extrapolated to predict differences in fracture efficacy. Head-to-head fracture studies have not been conducted.

A SIMILAR NUMBER OF STUDY PARTICIPANTS IN EACH TREATMENT GROUP REPORTED ADVERSE EVENTS DURING THE STUDY (78% PROLIA®, 79% ALENDRONATE)[4]

**SUMMARY OF ADVERSE EVENTS**

| | Alendronate (N = 249) n (%) | Prolia® (denosumab) (N = 253) n (%) |
|---|---|---|
| Any adverse event | 196 (78.7) | 197 (77.9) |
| Leading to study discontinuation | 2 (0.8) | 3 (1.2) |
| Death | 0 (0.0) | 1 (0.4) |
| Selected adverse events | | |
| Clinical fractures* | 4 (1.6) | 8 (3.2) |
| Gastrointestinal-related disorders | 60 (24.1) | 58 (22.9) |
| Infections | 93 (37.3) | 111 (43.9) |
| Neoplasms (benign or malignant) | 9 (3.6) | 9 (3.6) |
| Serious adverse events | 16 (6.4) | 15 (5.9) |
| Selected serious adverse events | | |
| Infections | 3 (1.2) | 1 (0.4) |
| Neoplasms (benign or malignant) | 3 (1.2) | 3 (1.2) |

The most frequent adverse events in the Prolia® and alendronate groups, respectively, were nasopharyngitis (13.4% and 10.8%), back pain (10.7% and 11.6%), bronchitis (6.3% and 5.6%), arthralgia (5.9% and 10.4%), constipation (5.1% and 4.8%), and pain in an extremity (4.7% and 8.4%).
*On-study clinical fractures were as follows: Prolia®—2 foot, 2 wrist, 1 radius, 1 fibula, 1 humerus, 1 pelvis, 1 rib, 1 tibia; alendronate—1 foot, 1 wrist, 1 radius, 1 sacrum.

Data used in USA-162-82078, Page 32

Kendler J Bone Miner Res 2010: 78/Table 2/Footnote

Data used in USA-162-82078, Page 32

Kendler J Bone Miner Res 2010: 78/A/Table 2

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

**Help lead your members to stronger bones with access to Prolia®.[1,4]**
**Please visit proliapayerresources.com for more information**

Links to: https://www.proliapayerresources.com/

Data from https://www.proliahcp.com/

Kendler J Bone Miner Res 2010: 79/B/2; Prolia PI v20 03/20: 23/A/2

Links to: https://www.mjhlifesciences.com/privacy

### 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.

**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


**References**: **1.** Prolia® (denosumab) prescribing information, Amgen. **2.** Cummings SR, San Martin J, McClung MR, Siris ES, Eastell R, Reid IR, et al. Denosumab for prevention of fractures in postmenopausal women with osteoporosis. *N Engl J Med* 2009;361:756-765. **3.** Bone HG, Wagman RB, Brandi ML, Brown JP, Chapurlat R, Cummings SR, et al. 10 years of denosumab treatment in postmenopausal women with osteoporosis: results from the phase 3 randomized FREEDOM trial and open-label extension. *Lancet Diabetes Endocrinol.* 2017;5:513-523. **4.** Kendler DL, Roux C, Benhamou CL, Brown JP, Lillestol M, Siddhanti S, et al. Effects of denosumab on bone mineral density and bone turnover in postmenopausal women transitioning from alendronate therapy. *J Bone Miner Res.* 2010;25:72-81.


Links to: https://www.amgen.com/privacy-statement/

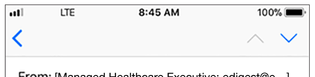
Links to: https://www.amgen.com/terms-of-use/

Links to: https://www.amgen.com/contact-us/



Links to: the user's external Outlook account to unsubscribe the user from emails

Email 2- MOBILE




From: [Managed Healthcare Executive; edigest@e…]

To: [Insert Customer Email]

Cc:

**Head-to-head Bone Mineral Density Study W..**

Yesterday at 6:25 PM

A

VARIABLE SUBJECT LINE OPTIONS:
1. [Bone Mineral Density Results for Prolia® vs Alendronate]
2. [Bone Mineral Density Results in Head-to-head Study of Prolia® vs Alendronate]
3. [Alendronate vs Prolia®: Bone Mineral Density Results in Women With Postmenopausal Osteoporosis]

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Managed Healthcare® EXECUTIVE

The following promotional message is brought to you by Amgen.

# Learn more about a head-to-head bone mineral density (BMD) comparing alendronate continuation to Prolia® in women with postmenopausal osteoporosis (PMO)

prolia® (denosumab) injection

## INDICATION

Prolia® (denosumab) 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],

### FREEDOM: Pivotal Phase 3 Fracture Trial

During the pivotal Phase 3 fracture trial in postmenopausal women with osteoporosis, Prolia® significantly reduced the relative risk of fracture at 3 years in vertebral, hip, and nonvertebral sites vs placebo.[1-3] Prolia® significantly increased bone mineral density at key sites at 3 years.[1,2]

Review 3-Year Pivotal FREEDOM Study

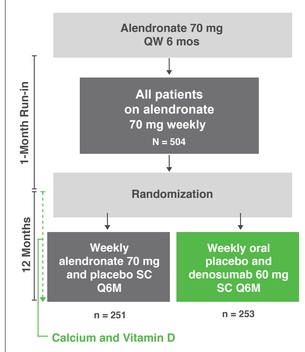
There were no significant differences between subjects who received Prolia® and those who received placebo in the total incidence of adverse events, serious adverse events, or the discontinuation of study treatment because of adverse events. The efficacy and safety of Prolia® in female patients with PMO were further evaluated in a 7-year open-label extension study.[3]

Review 10-year Open-label Extension Study

### STAND: Prolia® vs Alendronate

A head-to-head BMD study evaluated women with PMO continuing on alendronate or transitioning to Prolia® in a 1-year, multicenter, international, randomized, double-blind, double-dummy, parallel-group Phase 3 trial[4]

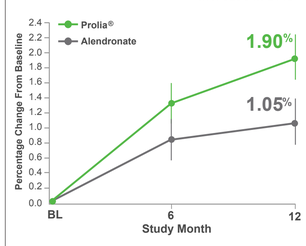
## PATIENTS CONTINUING ON ALENDRONATE THERAPY OR TRANSITIONING TO PROLIA® WERE EVALUATED[4]




Q6M=once every 6 months; QW=once a week; SC=subcutaneous.
Primary Endpoint: Percentage change in total hip BMD from baseline to month 12. Select Secondary Endpoint: Percentage change in BMD at lumbar spine at month 12. Study Population: Postmenopausal women with a BMD T-score of ≤ -2.0 and ≥ -4.0 at the lumbar spine or total hip. Women must have been receiving alendronate 70 mg/week for ≥ 6 months prior to screening.

## PROLIA® DEMONSTRATED NONINFERIORITY AND SUPERIORITY (VS ALENDRONATE) IN TOTAL HIP BMD[4]

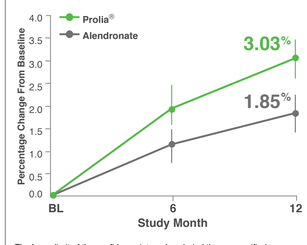
**0.85%*** increase in BMD




The lower limit of the confidence interval excluded the prespecified noninferiority margin (-0.35% for total hip), thus showing the noninferiority of Prolia® compared with alendronate.
Superiority testing demonstrated that the BMD increase with denosumab at the total hip was statistically superior to the change with alendronate ($P < 0.0001$).
*95% CI 0.44%-1.25%, $P < 0.01$.

## PROLIA® DEMONSTRATED NONINFERIORITY (VS ALENDRONATE) AND SHOWED STATISTICALLY SIGNIFICANT CHANGES IN LUMBAR SPINE BMD[4,*]

**1.18%†** increase in BMD




The lower limit of the confidence interval excluded the prespecified noninferiority margin (-0.22% for lumbar spine), thus showing the noninferiority of Prolia® compared with alendronate.
*Secondary endpoint.
†95% CI 0.63%-1.73%, $P < 0.01$.

BMD data results are not meant to imply fracture efficacy and should not be extrapolated to predict differences in fracture efficacy. Head-to-head fracture studies have not been conducted.

## A SIMILAR NUMBER OF STUDY PARTICIPANTS IN EACH TREATMENT GROUP REPORTED ADVERSE EVENTS DURING THE STUDY (78% PROLIA®, 79% ALENDRONATE)[4]

### SUMMARY OF ADVERSE EVENTS

| | Alendronate (N = 249) n (%) | Prolia® (denosumab) (N = 253) n (%) |
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The most frequent adverse events in the Prolia® and alendronate groups, respectively, were nasopharyngitis (13.4% and 10.8%), back pain (10.7% and 11.6%), bronchitis (6.3% and 5.6%), arthralgia (5.9% and 10.4%), constipation (5.1% and 4.8%), and pain in an extremity (4.7% and 8.4%).
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**Help lead your members to stronger bones with access to Prolia®.[1,4]**

**Please visit proliapayerresources.com for more information**

## 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®.

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**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.

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**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.

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

**References: 1.** Prolia® (denosumab) prescribing information, Amgen. **2.** Cummings SR, San Martin J, McClung MR, Siris ES, Eastell R, Reid IR, et al. Denosumab for prevention of fractures in postmenopausal women with osteoporosis. *N Engl J Med.* 2009;361:756-765. **3.** Bone HG, Chapurlat R, Brandi ML, Brown JP, Chapurlat R, Cummings SR, et al. The effect of three or six years of denosumab exposure in women with postmenopausal osteoporosis: results from the FREEDOM extension. *J Clin Endocrinol Metab.* 2013;98:4483-4492. **4.** Kendler DL, Roux C, Benhamou CL, et al. Effects of denosumab on bone mineral density and bone turnover in postmenopausal women transitioning from alendronate therapy. *J Bone Miner Res.* 2010;25:72-81.

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