PRIOR AUTHORIZATION POLICY

POLICY: Bone Modifiers – Prolia Prior Authorization Policy
- Prolia® (denosumab injection for subcutaneous use – Amgen)

REVIEW DATE: 07/29/2020

OVERVIEW

Prolia, a receptor activator of nuclear factor kappa-B (RANK) ligand inhibitor, is indicated for the following uses:[1]

- **Bone loss (treatment to increase bone mass), in men with nonmetastatic prostate cancer** at high risk for fracture receiving androgen deprivation therapy (ADT).
- **Bone loss (treatment to increase bone mass), in women with breast cancer** at high risk for fracture receiving adjuvant aromatase inhibitor (AI) therapy.
- **Glucocorticoid-induced osteoporosis** (treatment), in men and women at high risk of fracture who are either initiating or continuing systemic glucocorticoids in a daily dosage equivalent to 7.5 mg or greater of prednisone and expected to remain on glucocorticoids for at least 6 months.
- **Osteoporosis,** treatment of **postmenopausal women** at high risk of fracture.
- **Osteoporosis,** treatment to **increase bone mass in men** at high risk for fracture.

In general, high risk of fractures is defined as a history of osteoporotic fracture, multiple risk factors for fracture, or patients who have failed or are intolerant to other available osteoporosis therapy.[1] Of note, denosumab subcutaneous injection is also available under the brand name Xgeva®, and is indicated for the prevention of skeletal-related events in patients with multiple myeloma, as well as in patients with bone metastases from solid tumors, giant cell tumor of bone, and hypercalcemia of malignancy.[2]

Dosing Information

For all indications, the dose is 60 mg once every 6 months as a subcutaneous injection.[1]

Guidelines

Several guidelines address Prolia.

- **Breast Cancer/Prostate Cancer:** The National Comprehensive Cancer Network (NCCN) guidelines for breast cancer (version 5.2020 – July 15, 2020)[6] and prostate cancer (version 2.2020 – May 21, 2020)[7] note that if patients are receiving agents that impact bone mineral density (BMD), bisphosphonates (oral/intravenous), as well as Prolia, should be considered to maintain or improve BMD and/or reduce the risk of fractures.
- **Glucocorticoid-Induced Osteoporosis (GIO):** In 2017, the American College of Rheumatology (ACR) updated guidelines for the prevention and treatment of GIO.[5] In various clinical scenarios, oral bisphosphonates are preferred, followed by intravenous bisphosphonates (e.g., zoledronic acid injection).
- **Postmenopausal Osteoporosis:** Prolia is prominently featured in guidelines for postmenopausal osteoporosis by the Endocrine Society (2019)[3] and the American Association of Clinical Endocrinologists (AACE) and the American College of Endocrinology (ACE) [2020][4]. Prolia is one of among several agents cited as an alternative for patients at high risk for fractures.

POLICY STATEMENT
Prior authorization is recommended for prescription benefit coverage of Prolia. All approvals are provided for 1 year in duration. In the approval indication, as appropriate, an asterisk (*) is noted next to the specified gender. In this context, the specified gender is defined as follows: men are defined as individuals with the biological traits of a man, regardless of the individual's gender identity or gender expression.

Automation: Smart Coverage Review uses patient claim history to answer Prior Authorization questions regarding medication history of Boniva® (ibandronate injection for intravenous use) or Reclast® (zoledronic acid injection for intravenous use). A 2-year look back period will be used to check claim history and automate for use of either agent (Boniva intravenous or Reclast). If not in claims, medication history can be obtained through Prior Authorization criteria. For all reviews, other Prior Authorization criteria listed below will also be applied.

RECOMMENDED AUTHORIZATION CRITERIA
Coverage of Prolia is recommended in those who meet the following criteria:

FDA-Approved Indications

1. **Bone Loss (Treatment to Increase Bone Mass) in Patients with Breast Cancer at High Risk for Fracture Receiving Adjuvant Aromatase Inhibitor Therapy.** Approve for 1 year if the patient meets the following criteria (A and B):
   A) Patient has breast cancer that is not metastatic to bone; AND
   B) Patient is receiving aromatase inhibitor therapy (e.g., anastrozole, letrozole, or exemestane).

2. **Bone Loss (Treatment to Increase Bone Mass) in Patients with Nonmetastatic Prostate Cancer at High Risk for Fracture Receiving Androgen Deprivation Therapy.** Approve for 1 year if the patient meets the following criteria (A and B):
   A) Patient has prostate cancer that is not metastatic to bone; AND
   B) Patient meets ONE of the following conditions (i or ii):
      i. Patient is receiving androgen deprivation therapy (e.g., Lupron Depot® [leuprolide for depot suspension], Eligard® [leuprolide acetate for injectable suspension], Trelstar® [triptorelin pamoate for injectable suspension], or Zoladex® [goserelin implant]); OR
      ii. Patient has undergone bilateral orchiectomy.

3. **Glucocorticoid-Induced Osteoporosis – Treatment.** Approve for 1 year if the patient meets the following criteria (A and B):
   A) Patient is either initiating or continuing systemic glucocorticoids (e.g., prednisone); AND
   B) Patient meets ONE of the following (i, ii, iii, or iv):
      i. Patient has tried zoledronic acid injection (Reclast); OR
      ii. Patient has tried at least one oral bisphosphonate or oral bisphosphonate-containing product and meets one of the following (a, b, or c):
      Note: Examples of oral bisphosphonate products include Fosamax® (alendronate tablets and oral solution), Fosamax® Plus D (alendronate/cholecalciferol tablets), Actonel® (risedronate tablets), Atelvia® (risedronate delayed-release tablets), and Boniva® (ibandronate tablets).
         a) Patient has had an inadequate response to oral bisphosphonate therapy after a trial duration of 12 months as determined by the prescriber (e.g., ongoing and significant loss of bone mineral density [BMD], lack of BMD increase); OR

b) Patient has had an osteoporotic fracture or fragility fracture while receiving oral bisphosphonate therapy; OR
c) Patient has experienced intolerability to an oral bisphosphonate (e.g., severe gastrointestinal [GI]-related adverse effects, severe musculoskeletal-related side effects, a femoral fracture); OR

iii. Patient cannot take an oral bisphosphonate due to one of the following circumstances (a, b, or c):
a) Patient cannot swallow or has difficulty swallowing; OR
b) Patient cannot remain in an upright position post oral bisphosphonate administration; OR
c) Patient has a pre-existing gastrointestinal (GI) medical condition (e.g., patient with esophageal lesions, esophageal ulcers, or abnormalities of the esophagus that delay esophageal emptying [stricture, achalasia]); OR

iv. Patient meets one of the following conditions (a, b, or c):
a) Severe renal impairment (creatinine clearance < 35 mL/min); OR
b) Chronic kidney disease (CKD); OR
c) Patient has had an osteoporotic fracture or a fragility fracture.

4. Osteoporosis Treatment for a Postmenopausal Patient. Approve for 1 year if the patient meets the following criteria (A and B):

A) Patient meets ONE of the following conditions (i, ii, or iii):
i. Patient has had a T-score (current or at any time in the past) at or below -2.5 at the lumbar spine, femoral neck, total hip, and/or 33% (one-third) radius (wrist); OR
ii. Patient has had an osteoporotic fracture or a fragility fracture; OR
iii. Patient meets both of the following (a and b):
a) Patient has low bone mass (T-score [current or at any time in the past] between -1.0 and -2.5 at the lumbar spine, femoral neck, total hip and/or 33% [one-third] radius [wrist]); AND
b) Prescriber determines the patient is at high risk for fracture; AND

B) Patient meets ONE of the following (i, ii, iii, or iv):
i. Patient has tried ibandronate injection (Boniva) or zoledronic acid injection (Reclast); OR
ii. Patient has tried at least one oral bisphosphonate or oral bisphosphonate-containing product and meets one of the following (a, b, or c):
Note: Examples of oral bisphosphonate products include Fosamax® (alendronate tablets and oral solution), Fosamax® Plus D (alendronate/cholecalciferol tablets), Actonel® (risedronate tablets), Atelvia® (risedronate delayed-release tablets), and Boniva® (ibandronate tablets).
a) Patient has had an inadequate response to oral bisphosphonate therapy after a trial duration of 12 months as determined by the prescriber (e.g., ongoing and significant loss of bone mineral density (BMD), lack of BMD increase); OR
b) Patient has had an osteoporotic fracture or a fragility fracture while receiving oral bisphosphonate therapy; OR
c) Patient has experienced intolerability to an oral bisphosphonate (e.g., severe gastrointestinal-related adverse effects, severe musculoskeletal-related side effects, a femoral fracture); OR

iii. Patient cannot take an oral bisphosphonate due to one of the following circumstances (a, b, or c):
a) Patient cannot swallow or has difficulty swallowing; OR
b) Patient cannot remain in an upright position post oral bisphosphonate administration; OR
c) Patient has a pre-existing gastrointestinal medical condition (e.g., patient with esophageal lesions, esophageal ulcers, or abnormalities of the esophagus that delay esophageal emptying [stricture, achalasia]); OR

iv. Patient meets one of the following conditions (a, b, or c):
- **a)** Severe renal impairment (creatinine clearance < 35 mL/min); OR
- **b)** Chronic kidney disease (CKD); OR
- **c)** Patient has had an osteoporotic fracture or a fragility fracture.

5. Osteoporosis – Treatment (to Increase Bone Mass) for Men*. Approve for 1 year if the patient meets the following criteria (A and B):

A) Patient meets ONE of the following conditions (i, ii, or iii):
- **i.** Patient has had a T-score (current or at any time in the past) at or below -2.5 at the lumbar spine, femoral neck, total hip and/or 33% (one-third) radius (wrist); OR
- **ii.** Patient has had an osteoporotic fracture or a fragility fracture; OR
- **iii.** Patient meets both of the following (a and b):
  - **a)** Patient has low bone mass (T-score [current or at any time in the past] between -1.0 and -2.5 at the lumbar spine, femoral neck, total hip and/or 33% [one-third] radius [wrist]); AND
  - **b)** Prescriber determines the patient is at high risk of fracture; AND

B) Patient meets ONE of the following (i, ii, iii or iv):
- **i.** Patient has tried zoledronic acid injection (Reclast); OR
- **ii.** Patient has tried at least one oral bisphosphonate or oral bisphosphonate-containing product and meets one of the following (a, b, or c):
  Note: Examples of oral bisphosphonate products include Fosamax® (alendronate tablets and oral solution), Fosamax® Plus D (alendronate/cholecalciferol tablets), Actonel® (risedronate tablets), Atelvia® (risedronate delayed-release tablets), and Boniva® (ibandronate tablets).
  - **a)** Patient has had an inadequate response to oral bisphosphonate therapy after a trial duration of 12 months as determined by the prescriber (e.g., ongoing and significant loss of bone marrow density [BMD], lack of BMD increase); OR
  - **b)** Patient has had an osteoporotic fracture or a fragility fracture while receiving oral bisphosphonate therapy; OR
  - **c)** Patient has experienced intolerability to an oral bisphosphonate (e.g., severe gastrointestinal [GI]-related adverse effects, severe musculoskeletal-related side effects, a femoral fracture); OR
- **iii.** Patient cannot take an oral bisphosphonate due to one of the following circumstances (a, b or c):
  - **a)** Patient cannot swallow or has difficulty swallowing; OR
  - **b)** Patient cannot remain in an upright position post oral bisphosphonate administration; OR
  - **c)** Patient has a pre-existing GI medical condition (e.g., patient with esophageal lesions, esophageal ulcers, or abnormalities of the esophagus that delay esophageal emptying [stricture, achalasia]); OR
- **iv.** Patient meets one of the following conditions (a, b, or c):
  - **a)** Severe renal impairment (creatinine clearance < 35 mL/min); OR
  - **b)** Chronic kidney disease (CKD); OR
  - **c)** Patient has had an osteoporotic fracture or a fragility fracture.

* Refer to the Policy Statement.

CONDITIONS NOT RECOMMENDED FOR APPROVAL

Coverage of Prolia is not recommended in the following situations:

1. Concurrent Use with Other Medications for Osteoporosis.

Note: Examples include teriparatide injection for subcutaneous use (Forteo®/Bonsity®), Tymlos® (abaloparatide injection for subcutaneous use), oral bisphosphonates (e.g., alendronate, risedronate, ibandronate), intravenous bisphosphonates (zoledronic acid injection [Reclast], intravenous ibandronate), calcitonin nasal spray (Miacalcin®/Fortical®), and Evenity® (romosozumab-aqqg injection for subcutaneous use). Prolia is not indicated for use as combination therapy.[1]

2. **Giant Cell Tumor of Bone.** Studies with denosumab in giant cell tumor of the bone used dosing for Xgeva, which is indicated for the treatment of adults and skeletally mature adolescents with giant cell tumor of bone that is unresectable or where surgical resection is likely to result in severe morbidity.[2]
3. **Osteoporosis Prevention.** Prolia is not indicated for the prevention of osteoporosis.[1]

4. Coverage is not recommended for circumstances not listed in the Recommended Authorization Criteria. Criteria will be updated as new published data are available.

REFERENCES

1. Prolia® injection for subcutaneous use [prescribing information]. Thousand Oaks, CA: Amgen; March 2020.
2. Xgeva® injection for subcutaneous use [prescribing information]. Thousand Oaks, CA: Amgen; June 2020.
3. Eastell R, Rosen CJ, Black DM, et al. Pharmacological management of osteoporosis in postmenopausal women: an Endocrine Society clinical practice guideline. *J Clin Endocrinol Metab*. 2019;104(5):1595-1622. Available at: https://www.endocrine.org/guidelines-and-clinical-practice/clinical-practice-guidelines/osteoporosis-in-postmenopausal-women. Accessed on July 27, 2020.
4. Camacho PM, Petak SM, Binkley N, et al. American Association of Clinical Endocrinologists and American College of Endocrinology clinical practice guidelines for the diagnosis and treatment of postmenopausal osteoporosis-2020 update. *Endocrin Pract*. 2020;26(Suppl 1):1-46. Available at: https://journals.aace.com/doi/pdf/10.4158/GL-2020-0524SUPPL. Accessed on July 27, 2020.
5. Buckley L, Guyatt G, Fink HA, et al. 2017 American College of Rheumatology guideline for the prevention and treatment of glucocorticoid-induced osteoporosis. *Arthritis Rheumatol*. 2017;69(8):1521-1537. Available at: https://www.rheumatology.org/Portals/0/Files/Guideline-for-the-Prevention-and-Treatment-of-GIOP.pdf. Accessed on July 27, 2020.
6. The NCCN Breast Cancer Clinical Practice Guidelines in Oncology (Version 5.2020 – July 15, 2020). © 2020 National Comprehensive Cancer Network, Inc. Available at: http://www.nccn.org. Accessed on July 27, 2020.
7. The NCCN Prostate Cancer Clinical Practice Guidelines in Oncology (Version 2.2020 – May 21, 2020). © 2020 National Comprehensive Cancer Network, Inc. Available at: http://www.nccn.org. Accessed on July 27, 2020.