Medical Policy

BlueCross BlueShield of Kansas
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Title: Denosumab (Prolia and Xgeva)

- **BCBSKS will review Prior Authorization requests**

  Prior Authorization Form:
  http://www.bcbsks.com/CustomerService/Forms/pdf/15-17_predeterm_request_frm.pdf

  Link to Drug List (Formulary):
  http://www.bcbsks.com/CustomerService/PrescriptionDrugs/drug_list.shtml

Professional
Original Effective Date: April 30, 2012
Revision Date(s): August 14, 2012; March 12, 2013; August 1, 2016; May 10, 2017
Current Effective Date: May 10, 2017

Institutional
Original Effective Date: April 30, 2012
Revision Date(s): September 13, 2012; March 12, 2013; August 1, 2016; May 10, 2017
Current Effective Date: May 10, 2017

State and Federal mandates and health plan member contract language, including specific provisions/exclusions, take precedence over Medical Policy and must be considered first in determining eligibility for coverage. To verify a member's benefits, contact Blue Cross and Blue Shield of Kansas Customer Service.

The BCBSKS Medical Policies contained herein are for informational purposes and apply only to members who have health insurance through BCBSKS or who are covered by a self-insured group plan administered by BCBSKS. Medical Policy for FEP members is subject to FEP medical policy which may differ from BCBSKS Medical Policy.

The medical policies do not constitute medical advice or medical care. Treating health care providers are independent contractors and are neither employees nor agents of Blue Cross and Blue Shield of Kansas and are solely responsible for diagnosis, treatment and medical advice.

If your patient is covered under a different Blue Cross and Blue Shield plan, please refer to the Medical Policies of that plan.

DESCRIPTION

The intent of the denosumab medical drug criteria is to ensure appropriate selection of patients for treatment according to product labeling and/or clinical studies and/or guidelines and according to dosing recommended in product labeling. Patients considered candidates for therapy with these agents are appropriate patients with osteoporosis at high risk for fracture, appropriate patients at high risk for fracture receiving androgen

deprivation therapy for prostate cancer, appropriate patients at high risk for fracture receiving adjuvant aromatase inhibitor therapy for breast cancer, and patients with bone metastases from solid tumors.

These agents will not be approved for patients in whom it would be contraindicated. Because use of these agents in combination with other osteoporosis agents including bisphosphonates, SERMs (selective estrogen receptor modulator), and Forteo (teriparatide) has not been studied, the criteria will not approve combination therapy.

Target Drugs

- **Prolia** (denosumab)
- **Xgeva** (denosumab)

FDA Approved Indications and Dosages [1-2]

FDA Labeled Indications	Prolia (denosumab)	Xgeva (denosumab)
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 failed/intolerant to other osteoporosis therapy. Reduces incidence of vertebral, non-vertebral, and hip fractures.	60 mg subcutaneously every 6 months. All patients should receive 1000 mg daily of calcium and at least 400 IU vitamin D daily.	
Increase bone mass in men with osteoporosis at high risk for fracture, defined as a history of osteoporotic fracture, or multiple risk factors for fracture; or patients who failed/intolerant to other osteoporosis therapy.		
Increase bone mass in men at high risk for fracture receiving androgen deprivation therapy for nonmetastatic prostate cancer. Reduces incidence of vertebral fractures.		
Increase bone mass in women at high risk for fracture receiving adjuvant aromatase inhibitor therapy for breast cancer.		
Prevention of skeletal related events in patients with bone metastases from solid tumors.		120 mg subcutaneously every 4 weeks
Treatment of adults and skeletally mature adolescents with giant cell tumor of bone that is unresectable or resection likely to result in severe morbidity.		120 mg subcutaneously every 4 weeks with additional doses of 120 mg on Day 8 and 15 in first month of therapy
Treatment of hypercalcemia of malignancy refractory to bisphosphonate therapy		120 mg subcutaneously every 4 weeks with additional 120 mg doses on Days 8 and 15 of the first month of therapy

POLICY

PROLIA

Prolia will be approved when ALL of the following are met:

1. ONE of the following:
    a. BOTH of the following:
        i. The patient is a male, a postmenopausal female, **OR** the prescriber has provided documentation that the requested agent is medically appropriate for the patient's gender
        AND
        ii. The patient has a diagnosis of osteoporosis defined as ONE of the following:
            1. The patient has experienced previous vertebral fracture(s), or low trauma or fragility fracture(s) [e.g., prior fracture from minor trauma such as falling from standing height or less] within the past 5 years
            OR
            2. The patient has a T-score that is –2.5 or lower **AND** ONE of the following:
                i. The patient has failed a bisphosphonate
                OR
                ii. The patient has a documented intolerance, FDA labeled contraindication, or hypersensitivity to a bisphosphonate
                OR
                iii. BOTH of the following:
                    a. The patient is female **OR** the prescriber has provided documentation that SERM (selective estrogen receptor modulator) is medically appropriate for the patient's gender
                    AND
                    b. The patient has failed a SERM **OR** the patient has a documented intolerance, FDA labeled contraindication, or hypersensitivity to a SERM

    OR

b. The patient is requesting the agent for osteopenia (osteoporosis prophylaxis) **AND** ALL of the following:
   i. The patient is a male age 50 years of age and over, the patient is ~~a~~ postmenopausal, **OR** the prescriber has provided documentation that the requested agent is medically appropriate for the patient's gender
   AND
   ii. BOTH of the following:
      1. The patient has a T-score from -1.0 to -2.50
      AND
      2. 10-year probability of a hip fracture ≥ 3% per FRAX **OR** 10-year probability of a major OP-related fracture ≥ 20% per FRAX
   AND
   iii. ONE of the following:
      1. The patient has failed a bisphosphonate **OR** the patient has a documented intolerance, FDA labeled contraindication, or hypersensitivity to a bisphosphonate
      OR
      2. BOTH of the following:
         i. The patient is female **OR** the prescriber has provided documentation that SERM is medically appropriate for the patient's gender
         AND
         ii. The patient has failed a SERM **OR** the patient has a documented intolerance, FDA labeled contraindication, or hypersensitivity to SERM

OR

c. The patient has a diagnosis of breast cancer who is receiving aromatase inhibitor therapy **AND** ONE of the following:
   i. The patient has a history of vertebral fracture(s), or low trauma or fragility fracture(s) [e.g., prior fracture from minor trauma such as falling from standing height or less] within the past 5 years
   OR
   ii. The patient has a T-score of -1 or lower **AND** ONE of the following:
      1. The patient has failed a bisphosphonate
      OR
      2. The patient has a documented intolerance, FDA labeled contraindication, or hypersensitivity to a bisphosphonate

OR

d. The patient has a diagnosis of nonmetastatic prostate cancer receiving androgen deprivation therapy (ADT) **AND** ONE of the following:
    i. The patient has a history of vertebral fracture(s), or low trauma or fragility fracture(s) [e.g., prior fracture from minor trauma such as falling from standing height or less] within the past 5 years
    OR
    ii. BOTH of the following:
        1. ONE of the following:
            a. The patient is ≥70 years of age
            OR
            b. The patient is <70 years of age AND ONE of the following:
                i. The patient has a T-score of -1 or lower
                OR
                ii. The patient has a history of an osteoporotic fracture
        AND
        2. The patient has failed a bisphosphonate **OR** the patient has a documented intolerance, FDA labeled contraindication, or hypersensitivity to a bisphosphonate

AND

2. BOTH of the following:
    a. The patient's calcium level has been measured in the past 4 weeks
    AND
    b. If the patient is hypocalcemic, it will be corrected prior to initiating Prolia

AND

3. ONE of the following:
    a. The patient is not receiving concomitant Xgeva (denosumab), bisphosphonate, SERM, or Forteo (teriparatide) therapy
    OR
    b. The prescriber indicates that the patient will discontinue the current Xgeva (denosumab), bisphosphonate, SERM, or Forteo (teriparatide) prior to initiation of the requested agent

AND

4. The patient does not have any FDA labeled contraindication(s) to therapy with the requested agent

Length of approval: 12 months

XGEVA

Xgeva will be approved when ALL the following are met:

1. **ONE** of the following:
    a. The patient has a solid tumor cancer diagnosis (e.g. thyroid, non-small cell lung, or kidney cancer, prostate cancer, breast cancer) and ALL of the following:
        i. The patient has documented bone metastases
        AND
        ii. The patient has a life expectancy ≥ 3 months
        AND
        iii. ONE of the following:
            a. The patient has failed zoledronic acid
            OR
            b. The patient has a documented intolerance, FDA labeled contraindication or hypersensitivity to zoledronic acid
        AND
        iv. BOTH of the following:
            a. The patient's calcium levels have been measured within the last 4 weeks
            AND
            b. If the patient is hypocalcemic, it will be corrected prior to initiating Xgeva

    OR

    b. The patient has a diagnosis of giant cell tumor of bone and ALL of the following:
        i. The patient is an adult or skeletally mature adolescent (must be ≥13 years of age)
        AND
        ii. ONE of the following:
            a. The tumor is recurrent
            OR
            b. The tumor is unresectable
            OR
            c. Resection is likely to result in severe morbidity
        AND
        iii. BOTH of the following:
            a. The patient's calcium levels have been measured within the last 4 weeks
            AND
            b. If the patient is hypocalcemic, it will be corrected prior to initiating Xgeva

    OR

c. The patient has a diagnosis of hypercalcemia of malignancy and BOTH of the following:
    i. ONE of the following:
        a. The patient has failed/is refractory to intravenous bisphosphonate therapy (i.e. albumin-corrected calcium of ≥ 12.5 mg/dL [3.1 mmol/L])
        OR
        b. The patient has a documented intolerance, FDA labeled contraindication, or hypersensitivity to intravenous bisphosphonate therapy
    AND
    ii. ONE of the following:
        a. The patient has failed zoledronic acid
        OR
        b. The patient has a documented intolerance, FDA labeled contraindication or hypersensitivity to zoledronic acid

AND

2. ONE of the following:
    a. The patient is not receiving concomitant Prolia therapy
    OR
    b. The prescriber indicates that the patient will discontinue Prolia prior to beginning therapy with Xgeva

AND

3. The agent is NOT being prescribed for prevention of skeletal-related events secondary to multiple myeloma

AND

4. The patient does not have any FDA labeled contraindication(s) to therapy with the requested agent

Length of approval: 12 months

RATIONALE

Denosumab is a receptor activator or nuclear factor K-β ligand (RANKL) inhibitor. RANKL is a transmembrane (soluble protein) essential for the formation, function, and survival of osteoclasts, the cells responsible for bone resorption. Increased osteoclast activity, stimulated by RANKL, is a mediator for bone pathology in solid tumors with osseous metastases.[1] Prevention of the RANK/RANKL interaction inhibits osteoclast formation, function, and survival, thereby decreasing bone resorption and increasing bone mass and strength in both cortical and trabecular bone.[2]

Hypocalcemia is contraindicated when using denosumab. The patient's calcium level should be corrected prior to use. This agent should not be used in pregnancy as it may cause fetal harm. Osteonecrosis of the jaw (ONJ) has been reported with the use of denosumab. A routine oral exam should be performed by the prescriber prior to therapy initiation and appropriate preventive dentistry should be considered prior to therapy in patients with risk factors for ONJ. Good oral hygiene should be maintained during therapy with denosumab.[1, 2]

Postmenopausal Osteoporosis

The diagnosis of osteoporosis (OP) has been established by measurement of bone mineral density (BMD). BMD appears to be a predictor of fractures. BMD is expressed in absolute terms of grams of mineral per square centimeter scanned (g/cm^2) and as a relationship to two norms: compared to the expected BMD for the patient's age and sex (Z-score), or compared to "young normal" adults of the same sex (T-score).[3] The difference between the patient's score and the norm is expressed in standard deviations (SD) above or below the mean. Usually, 1 SD equals 10 to 15% of the BMD value in g/cm^2. The North American Menopause Society (NAMS)[4], World Health Organization (WHO)[5], International Society of Clinical Densitometry[6], and the National Osteoporosis Foundation (NOF)[3] define OP in postmenopausal women or a man ≥50 years old as a BMD T-score ≤ -2.5 at the total hip, femoral hip, or lumbar spine (≥ 2 vertebral levels measured in the posterior-anterior projection not the lateral projection).[3,5,6] In addition to diagnosis through densitometry, OP can be diagnosed clinically, regardless of the T-score. The presence of fragility fracture constitutes a clinical diagnosis of OP.[4]

BMD-based definitions of bone density [3,4-5]

Normal……T-score ≥ -1.0
Low bone mass……T-score between -1.0 and -2.5 (osteopenia)
Osteoporosis……T-score ≤ -2.5

The NAMS and NOF as well as the American Association of Clinical Endocrinologists (AACE) recommend adding OP drug therapy in the following populations:[3,4,7]

- All men and postmenopausal women who have had an osteoporotic vertebral or hip fracture
- All men and postmenopausal women who have BMD values consistent with OP (i.e., T-scores < -2.5) at the lumbar spine, femoral neck, or total hip region.
- All men age 50 and older, and postmenopausal women who have T-scores from -1.0 to -2.5 at the femoral neck, total hip, or lumbar spine by DXA and a 10-year probability of a hip fracture ≥ 3% or a 10-year probability of a major OP-related fracture ≥ 20% based on the U.S.-adapted WHO absolute fracture risk model (FRAX).

Patients with a fragility fracture of the spine or hip are at very high risk for another fracture regardless of whether the T-score is below -2.5 or just in the osteopenia range.[8] Alendronate has been found to be effective for secondary prevention of vertebral, non-vertebral, hip, and wrist fractures, but only effective for primary prevention of vertebral fractures in postmenopausal women in a meta-analysis of 11 trials which included 12,068 women.[20] Although bone densitometry is useful for assessing disease severity and monitoring therapy in patients with fractures, densitometry is not essential for the diagnosis of osteoporosis in this setting.[8]

The risk for a second fragility fracture decreases as time passes from the first fracture.[9,10] The study by Johnell et al. found that for all fractures, more fractures occurred in the first year after fracture than in subsequent years. The number of fractures decreased progressively thereafter with time.[9] Schousboe et al. found that prior non-spine non-hip fracture confers a modest excess risk for incident hip fracture independent of BMD after 10 years; that excess risk, however, was only about one third the excess risk during the first 5 years of follow-up.[10]

Guidelines from the American Association of Clinical Endocrinologists (AACE)[3] and the American College of Obstetricians and Gynecologists (ACOG)[11] state that although evidence for the efficacy in reducing the risk of new vertebral fractures is available for all of the agents approved for the treatment of osteoporosis (alendronate, ibandronate, risedronate, zoledronic acid (5 mg/100 mL), calcitonin, denosumab (60mg/mL), raloxifene, and teriparatide), only alendronate, risedronate, zoledronic acid, denosumab, and teriparatide reduce the risk of non-vertebral fractures. Alendronate, risedronate, zoledronic acid, and denosumab have demonstrated reduction of the risk of hip fractures in prospective controlled osteoporosis trials.[3,11]

The AACE recommends alendronate, risedronate, zoledronic acid, or denosumab as first line agents, ibandronate as a second line agent, raloxifene as a second or third line agent, and calcitonin as the last line agent. Teriparatide is best used in treating women with osteoporosis who are at high risk for fracture.[3]

Regarding combination therapy, the AACE guidelines state: There are no studies showing that combination treatment with 2 or more osteoporosis drugs has a greater effect on fracture reduction than treatment with a single agent. Modest additive effects on BMD and bone turnover have been observed with combinations of 2 antiresorptive agents. The combined use of an antiresorptive drug and teriparatide or parathyroid hormone (PTH) may alter the BMD and bone turnover response, depending on which antiresorptive agent is used. Combination therapy substantially increases the cost and probably increases the potential for side effects. Until the effect of combination therapy on fracture risk is better understood, AACE does not recommend concomitant use of these agents for prevention or treatment of postmenopausal osteoporosis.[3]

Osteoporosis in Men

The Endocrine Society 2012 Clinical Practice Guideline: Osteoporosis in Men recommends the following[12]: Men at high risk of fracture be treated with medication approved by regulatory agencies such as the U.S. FDA or the European Medicines Agency (EMA) (at the time of this writing, alendronate, risedronate, zoledronic acid, and teriparatide; also denosumab for men receiving ADT [androgen deprivation therapy] for prostate cancer) and that the selection of therapeutic agent be individualized based on factors including fracture history, severity of osteoporosis (T-scores), and the risk for hip fracture. [12]

Breast Cancer
The National Comprehensive Cancer Network (NCCN) Guidelines in Oncology-Breast Cancer 2016[13] state that:

- NCCN Guidelines-Recurrent or Stage IV Invasive Breast Cancer: Denosumab (Xgeva), zoledronic acid (Zometa) or pamidronate (all with calcium/vitamin D supplementation) should be given (Category 1) in addition to chemotherapy or endocrine therapy if bone metastasis is present, expected survival is >3 months, and renal function is adequate.
- NCCN Compendium
  - Denosumab: Denosumab (Xgeva) recommended as part of treatment for invasive breast cancer (Category 1).

The American Society of Clinical Oncology (ASCO) Update on the Role of Bisphosphonates and Bone Health Issus in Women with Breast Cancer[14,15] states that most women with newly diagnosed breast cancer are at risk of osteoporosis either because of their age or their breast cancer treatment. The update contains an algorithm for patient management. According to the algorithm, the following are considered factors for high risk: age >65 years; age 60-64 years and prior fracture, body weight <70 kg, family history; postmenopausal women of any age receiving aromatase inhibitor therapy; and premenopausal women with therapy associated premature menopause. Bisphosphonate is recommended for women at high risk with a T score of -2.5 or lower.[14]

Prostate Cancer
The NCCN Guidelines in Oncology-Prostate Cancer 2016[16] state that:

- NCCN Compendium
  - Denosumab: Denosumab (Xgeva) recommended as part of treatment for invasive prostate cancer (Category 1). Denosumab (Prolia) for prostate cancer androgen deprivation therapy (2A).
- NCCN Guidelines-Prostate Cancer (2016):Zoledronic acid or denosumab is recommended for men with castration resistant prostate cancer (CRPC) and bone metastases to prevent/delay disease associated skeletal related events [Category 1] (e.g., pathologic fracture, spinal cord compression, operation, or external beam radiation therapy to bone).
  - In patients on androgen deprivation therapy (ADT), denosumab (60 mg subcutaneous every 6 months), zoledronic acid (5 mg IV annually), or alendronate (70 mg weekly) is recommended when the absolute fracture risk warrants drug therapy (Category 2A).

Solid Tumor
The NCCN Guidelines in Oncology for several solid tumor types (i.e. thyroid[17], non-small cell lung cancer[18], kidney cancer[19]) recommend bisphosphonates (e.g. pamidronate or zoledronic acid) or denosumab as therapeutic options to treat bone metastases.

CODING

The following codes for treatment and procedures applicable to this policy are included below for informational purposes. Inclusion or exclusion of a procedure, diagnosis or device code(s) does not constitute or imply member coverage or provider reimbursement. Please refer to the member's contract benefits in effect at the time of service to determine coverage or non-coverage of these services as it applies to an individual member.

CPT/HCPCS

J0897	Injection, denosumab, 1 mg

DIAGNOSES

Prolia

ICD-10

C61	Malignant neoplasm of prostate
M81.0	Age-related osteoporosis without current pathological fracture
T50.905A	Adverse effect of unspecified drugs, medicaments and biological substances, initial encounter
T50.905D	Adverse effect of unspecified drugs, medicaments and biological substances, subsequent encounter
T50.905S	Adverse effect of unspecified drugs, medicaments and biological substances, sequela
Z79.811	Long term (current) use of aromatase inhibitors
Z87.311	Personal history of (healed) other pathological fracture
Z87.312	Personal history of (healed) stress fracture
Z87.81	Personal history of (healed) traumatic fracture

ICD-9

733.01	Senile osteoporosis
E933.6	Primarily systemic agents; oral bisphosphonates
V07.52	Use of agents affecting estrogen receptors and estrogen levels; use of aromatase inhibitors
V13.51	Other musculoskeletal disorders; pathologic fracture

Xgeva

ICD-10

C33	Malignant neoplasm of trachea
C34.01	Malignant neoplasm of right main bronchus
C34.02	Malignant neoplasm of left main bronchus
C34.11	Malignant neoplasm of upper lobe, right bronchus or lung
C34.12	Malignant neoplasm of upper lobe, left bronchus or lung
C34.2	Malignant neoplasm of middle lobe, bronchus or lung
C34.31	Malignant neoplasm of lower lobe, right bronchus or lung
C34.32	Malignant neoplasm of lower lobe, left bronchus or lung
C34.81	Malignant neoplasm of overlapping sites of right bronchus and lung
C34.82	Malignant neoplasm of overlapping sites of left bronchus and lung
C40.01	Malignant neoplasm of scapula and long bones of right upper limb
C40.02	Malignant neoplasm of scapula and long bones of left upper limb

C40.11	Malignant neoplasm of short bones of right upper limb
C40.12	Malignant neoplasm of short bones of left upper limb
C40.21	Malignant neoplasm of long bones of right lower limb
C40.22	Malignant neoplasm of long bones of left lower limb
C40.31	Malignant neoplasm of short bones of right lower limb
C40.32	Malignant neoplasm of short bones of left lower limb
C40.81	Malignant neoplasm of overlapping sites of bone and articular cartilage of right limb
C40.82	Malignant neoplasm of overlapping sites of bone and articular cartilage of left limb
C40.91	Malignant neoplasm of unspecified bones and articular cartilage of right limb
C40.92	Malignant neoplasm of unspecified bones and articular cartilage of left limb
C41.0	Malignant neoplasm of bones of skull and face
C41.1	Malignant neoplasm of mandible
C41.2	Malignant neoplasm of vertebral column
C41.3	Malignant neoplasm of ribs, sternum and clavicle
C41.4	Malignant neoplasm of pelvic bones, sacrum and coccyx
C41.9	Malignant neoplasm of bone and articular cartilage, unspecified
C73	Malignant neoplasm of thyroid gland
C79.51	Secondary malignant neoplasm of bone
C79.52	Secondary malignant neoplasm of bone marrow
E83.52	Hypercalcemia

ICD-9

198.5	Secondary malignant neoplasm of other specified sites; bone and bone marrow

REVISIONS	
08-14-2012	Policy added to the bcbsks.com web site.
03-12-2013	In Description section: ▪ Added the Prolia FDA Indication, “4. Treatment to increase bone mass in men with osteoporosis at high risk of fracture.”
	In Policy section: ▪ Added in A. Prolia the medically necessary indication of: "4. Treatment of osteoporosis (T-score below -2.5) in men who have failed or are unable to tolerate oral bisphosphonates [e.g. alendronate (Fosamax), risedronate (Actonel), ibandronate (Boniva)]." ▪ In the Policy Guidelines removed from item 3, "... in men who are not receiving androgen deprivation therapy or..." to read, "In the absence of safety data, using denosumab for the treatment of osteoporosis in premenopausal women or children is not recommended." ▪ Added guideline "8. Men seem to respond to available therapies in the same way that women respond. Bisphosphonates are considered the treatment of choice for most men with osteoporosis requiring pharmacologic therapy. Denosumab is an alternative option for men who cannot tolerate oral or intravenous bisphosphonates."
	Rationale section updated
	References updated
08-01-2016	Policy published 07-01-2016. Policy effective 08-01-2016.
	In Description section

REVISIONS	
	▪ Updated Description to include updates to FDA Indication chart and Dosing information
	In Policy section: Prolia ▪ Updated to current criteria and removed: "Prolia is considered medically necessary for the following indications: 1. Treatment of osteoporosis (T-score below -2.5) in postmenopausal women who have failed or are unable to tolerate oral bisphosphonates [e.g. alendronate (Fosamax), risedronate (Actonel), ibandronate (Boniva)]. 2. Treatment of bone loss in women receiving aromatase inhibitor (AI) therapy for breast cancer and have failed or are unable to tolerate oral bisphosphonates [e.g. alendronate (Fosamax), risedronate (Actonel), ibandronate (Boniva)]. 3. Treatment of bone loss in men receiving androgen deprivation therapy (ADT) for nonmetastatic prostate cancer. 4. Treatment of osteoporosis (T-score below -2.5) in men who have failed or are unable to tolerate oral bisphosphonates [e.g. alendronate (Fosamax), risedronate (Actonel), ibandronate (Boniva)]." Xgeva "Xgeva is considered medically necessary for the prevention of skeletal-related events (e.g., fracture, spinal cord compression, bone pain requiring surgery / radiation therapy) in patients with bone metastases from solid tumors." ▪ Removed Policy Guidelines 1. Given the absence of long-term safety data and availability of other agents, denosumab is not recommended for the prevention of osteoporosis. 2. For postmenopausal women with uncomplicated osteoporosis (T-score below -2.5), denosumab is not recommended as initial therapy. Oral bisphosphonates are preferred as initial therapy because of their efficacy, favorable cost, and the availability of long-term safety data. 3. In the absence of safety data, using denosumab for the treatment of osteoporosis in premenopausal women or children is not recommended. 4. Patients who have hypocalcemia should not receive denosumab until hypocalcemia is corrected. 5. Patients with chronic kidney disease (creatinine clearance <30 mL/min, including patients receiving dialysis) are at higher risk for hypocalcemia following denosumab administration than patients with normal renal function. 6. Because serious infections and skin reactions were reported more frequently in the denosumab than in the placebo group, patients should be advised to seek medical attention if they develop signs of an infection or skin reaction. 7. Additional recommendations include administration of calcium 1000 mg daily and at least 400 IU of vitamin D daily. 8. Men seem to respond to available therapies in the same way that women respond. Bisphosphonates are considered the treatment of choice for most men with osteoporosis requiring pharmacologic therapy. Denosumab is an alternative option for men who cannot tolerate oral or intravenous bisphosphonates." ▪ Removed Documentation recommendations: "Prolia - DEXA report and clinical records to include medication history Xgeva - Clinical records documenting bone metastases"

REVISIONS	
	Rationale section added
	In Coding section: ▪ Added ICD-10 codes: Prolia - C61, M81.0, T50.905A, T50.905D, T50.905S, Z79.811, Z87.311, Z87.312, Z87.81 Xgeva - C33, C34.01, C34.02, C34.11, C34.12, C34.2, C34.31, C34.32, C34.81, C34.82, C40.01, C40.02, C40.11, C40.12, C40.21, C40.22, C40.31, C40.32, C40.81, C40.82, C40.91, C40.92, C41.0, C41.1, C41.2, C41.3, C41.4, C41.9, C73, C79.51, C79.52, E83.52
	References updated
05-10-2017	Description section updated
	In Policy section: Prolia ▪ In Item 1 a i added "the prescriber has provided documentation that the requested agent is medically appropriate for the patient's gender" to read "The patient is a male, a postmenopausal female, OR the prescriber has provided documentation that the requested agent is medically appropriate for the patient's gender" ▪ In Item 1 a ii added "The patient has" and removed "with" to read "The patient has a diagnosis of osteoporosis defined as ONE of the following:" ▪ In Item 1 a ii 1 revised "a history of" to "experienced previous" ▪ In Item 1 a ii 2 i removed "is female and", "either", "or selective estrogen receptor (SERM)" to read "The patient has failed a bisphosphonate" ▪ In Item 1 a ii 2 added "The patient has a documented intolerance, FDA labeled contraindication, or hypersensitivity to a bisphosphonate OR iii. BOTH of the following: a. The patient is female OR the prescriber has provided documentation that SERM (selective estrogen receptor modulator) is medically appropriate for the patient's gender AND" ▪ In Item 1 a ii 2 iii b added "The patient has failed a SERM" and removed "The patient is male and has failed a bisphosphonate" to read "The patient has failed a SERM OR the patient has a documented intolerance, FDA labeled contraindication, or hypersensitivity to a SERM" ▪ In Item 1 b i added "OR the prescriber has provided documentation that the requested agent is medically appropriate for the patient's gender" and removed "woman" to read "The patient is a male age 50 years of age and over, the patient is postmenopausal, OR the prescriber has provided documentation that the requested agent is medically appropriate for the patient's gender" ▪ In Item 1 b iii 1 removed "is female and", "or SERM", "The patient is male and has failed a bisphosphonate OR", and "a SERM" to read "The patient has failed a bisphosphonate OR the patient has a documented intolerance, FDA labeled contraindication, or hypersensitivity to a bisphosphonate" ▪ In Item 1 b iii added "BOTH of the following: i. The patient is female OR the prescriber has provided documentation that SERM is medically appropriate for the patient's gender AND ii. The patient has failed a SERM OR the patient has a documented intolerance,

REVISIONS	
	FDA labeled contraindication, or hypersensitivity to a SERM" ▪ In Item 1 c added "has" and removed "is a woman with" to read "The patient has a diagnosis of breast cancer who is receiving aromatase inhibitor therapy AND ONE of the following:" ▪ In Item 1 d added "has" and "nonmetastatic" and removed "is a man with" to read "The patient has a diagnosis of nonmetastatic prostate cancer receiving androgen deprivation therapy (ADT) AND ONE of the following:" ▪ In Item 3 a removed "in the past 30 days" to read "The patient is not receiving concomitant Xgeva (denosumab), bisphosphonate, SERM, or Forteo (teriparatide) therapy" ▪ In Item 3 b added "prior to initiation of the requested agent" and removed "therapy" to read "The prescriber indicates that the patient will discontinue the current Xgeva (denosumab), bisphosphonate, SERM, or Forteo (teriparatide) prior to initiation of the requested agent" <u>Xgeva</u> ▪ In Item 1 a iv a added "measured within the last 4 weeks" and removed "tested" to read "The patient's calcium levels have been measured within the last 4 weeks"
	Rationale section updated
	References updated

REFERENCES

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