Pharmacy Policy Bulletin: J-0615 Denosumab Products for Bone Disease and Evenity (romosozumab-aqqg) – Commercial and Healthcare Reform	
Number: J-0615	**Category:** Prior Authorization
Line(s) of Business: ☒ Commercial ☒ Healthcare Reform ☐ Medicare	**Benefit(s):** **Commercial:** **Prior Authorization (1.):** **1.** Miscellaneous Specialty Drugs Injectable = Yes w/ Prior Authorization **Healthcare Reform:** Not Applicable
Region(s): ☒ All ☐ Delaware ☐ New York ☐ Pennsylvania ☐ West Virginia	**Additional Restriction(s):** None
Version: J-0615-015	**Original Date:** 08/09/2017
Effective Date: 10/08/2025	**Review Date:** 09/17/2025

Drugs Product(s):	• Conexxence (denosumab-bnht) • Evenity (romosozumab-aqqg) • Jubbonti (denosumab-bbdz) • Prolia (denosumab) • Stoboclo (denosumab-bmwo)

FDA-Approved Indication(s):	• Denosumab
	  ○ 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.
	  ○ Treatment to 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 have failed or are intolerant to other available osteoporosis therapy.
	  ○ Treatment of glucocorticoid-induced osteoporosis 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. High risk of fracture 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.
	  ○ Treatment to increase bone mass in men at high risk for fracture receiving androgen deprivation therapy for nonmetastatic prostate cancer.
	  ○ Treatment to increase bone mass in women at high risk for fracture receiving adjuvant aromatase inhibitor therapy for breast cancer.
	• Evenity (romosozumab-aqqg)
	  ○ Treatment of osteoporosis in postmenopausal women 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.

Background:

Class	Drug(s)
Antiresorptive Agents	
Bisphosphonates: bind to the surfaces of the bones and slow down the bone resorption action of the osteoclasts (bone-eroding cells). This allows the osteoblasts (bone-building cells) to work more effectively.	alendronate ibandronate risedronate zoledronic acid
RANK ligand (RANKL) Inhibitor: inhibits the development and activation of osteoclasts (the cells that eat away bone).	Conexxence (denosumab-bnht) Jubbonti (denosumab-bbdz) Prolia (denosumab) Stoboclo (denosumab-bmwo)
Estrogen Therapy or Hormone Therapy: prevents bone resorption	Estrogens, selective estrogen receptor modulators (SERMs), calcitonin
Anabolic Agents	
Sclerostin Inhibitor: increases bone mineral density in both the lumbar spine and total hip, and in both trabecular and cortical bone, leading to an increase in bone strength and reduced risk of fracture.	Evenity (romosozumab-aqqg): Limit duration of use to 12 monthly doses. If osteoporosis therapy remains warranted, continued therapy with an anti-resorptive agent should be considered.
Parathyroid Hormone (PTH) Analog: works on the bone remodeling (bone is constantly renewed) process so that new bone is generated and added to the skeleton faster than old bone is broken down. It does this by activating the osteoblast (bone-building) cells.	Teriparatide: Use for more than 2 years during a patient's lifetime should only be considered if a patient remains at or has returned to having a high risk for fracture.
Parathyroid Hormone-Related Protein (PTHrp) Analog: binds to one of the PTH receptors in your bone promoting bone formation and minimizes the other function of PTH, namely bone resorption, and calcium release.	Tymlos (abaloparatide): Use for more than 2 years during a patient's lifetime is not recommended.

- Bone mineral density (BMD) testing generates a T-score and is a powerful tool that diagnoses osteopenia and osteoporosis. A score T-score of -1 to greater than -2.5 indicates osteopenia, and a score of -2.5 or less indicates osteoporosis.
- Clinical risk factors also significantly influence fracture risk in individual patients. The Fracture Risk Assessment Tool (FRAX) tool incorporates multiple clinical risk factors that predict fracture risk, largely independent of BMD. Clinical risk factors in FRAX include age, sex, body mass index, smoking, alcohol use, prior fracture, parental history of hip fracture, use of glucocorticoids, rheumatoid arthritis, secondary osteoporosis, and femoral neck BMD, when available.
- The 2020 Endocrine Society guideline for Pharmacological Management of Osteoporosis in Postmenopausal Women defines fracture risk as follows:

Low Risk	○ No prior hip or spine fractures, **and** ○ BMD T-score at the hip and spine both > −1.0, **and** ○ 10-year hip fracture risk < 3%, **and** ○ 10-year major osteoporotic fracture risk < 20%
Moderate Risk	○ No prior hip or spine fractures, **and**

	○ BMD T-score at the hip and spine both > −2.5, **and** ○ 10-year hip fracture risk < 3%, **and** ○ 10-year major osteoporotic fracture risk < 20%
High Risk	○ Prior spine or hip fracture, **or** ○ BMD T-score at the hip or spine ≤ −2.5, **or** ○ 10-year hip fracture risk ≥ 3%, **or** ○ 10-year major osteoporotic fracture risk ≥ 20%
Very High Risk	○ Multiple spine fractures, **and** ○ BMD T-score at the hip or spine ≤ −2.5

- The 2023 Pharmacologic Treatment of Primary Osteoporosis or Low Bone Mass to Prevent Fractures in Adults: A Living Clinical Guideline from the American College of Physicians (ACP) recommends the following:
  - ACP recommends that clinicians use bisphosphonates for initial pharmacologic treatment to reduce the risk of fractures in postmenopausal females diagnosed with primary osteoporosis (strong recommendation; high-certainty evidence).
  - ACP suggests that clinicians use bisphosphonates for initial pharmacologic treatment to reduce the risk of fractures in males diagnosed with primary osteoporosis (conditional recommendation; low-certainty evidence).
  - ACP suggests that clinicians use the RANK ligand inhibitor (denosumab) as a second-line pharmacologic treatment to reduce the risk of fractures in postmenopausal females diagnosed with primary osteoporosis who have contraindications to or experience adverse effects of bisphosphonates (conditional recommendation; moderate-certainty evidence).
  - ACP suggests that clinicians use the RANK ligand inhibitor (denosumab) as a second-line pharmacologic treatment to reduce the risk of fractures in males diagnosed with primary osteoporosis who have contraindications to or experience adverse effects of bisphosphonates (conditional recommendation; low-certainty evidence).
  - ACP suggests that clinicians use the sclerostin inhibitor (romosozumab, moderate-certainty evidence) or recombinant parathyroid hormone (teriparatide, low-certainty evidence), followed by a bisphosphonate, to reduce the risk of fractures only in females with primary osteoporosis with very high risk of fracture (conditional recommendation).
  - ACP suggests that clinicians take an individualized approach regarding whether to start pharmacologic treatment with a bisphosphonate in females over the age of 65 with low bone mass (osteopenia) to reduce the risk of fractures (conditional recommendation; low-certainty evidence).”
- Both the 2020 Endocrine Society and the 2023 ACP guidelines recommend romosozumab as first line treatment for patients with osteoporosis at very high risk for a fracture. Bisphosponates and denosumab are recommended as potential treatment options following romosozumab.
- ICD-10 Code Information:
  - ICD-10: M85.8 “Other specified disorders of bone density and structure” may apply to osteopenia; however, the prescriber must confirm that the member has a specific diagnosis of osteopenia.
- Prescribing Considerations:
  - Screening for underlying causes of secondary osteoporosis such as hyperthyroidism or hyperparathyroidism, hypogonadism, chronic estrogen deficiency state (for example, menopause before age 45,

	bilateral oophorectomy), vitamin D deficiency, chronic liver disease or chronic kidney disease is recommended. ○ Postmenopausal females with osteopenia and risk factors are recommended to consider osteoporosis treatment. ○ It is recommended that the member is taking calcium and vitamin D supplements daily. ○ Pregnancy should be ruled out prior to administration of denosumab products for bone disease. ○ Bisphosphonate therapy is contraindicated in patients with creatinine clearance less < 35 mL/min, hypocalcemia, esophageal ulcerations, esophageal stricture, Barrett's esophagus, and active ulcers.

Approval Criteria

I. Approval Criteria

A. Denosumab Products for Bone Disease

1. Non-Metastatic Prostate Cancer or Breast Cancer

When a benefit, coverage of denosumab products for bone disease may be approved when one (1) of the following criteria is met **(a. or b.)**:

a. The member is male and all of the following criteria are met **(i. through iv.)**:
- **i.** The member has a diagnosis of prostate cancer (ICD-10: C61) that is nonmetastatic.
- **ii.** The member has a T-score ≤ -1.0 and one (1) of the following criteria is met **(A) or B))**:
  - **A)** The member has multiple risk factors for a fracture.
  - **B)** The member has experienced a previous fragility fracture.
- **iii.** The member is receiving androgen deprivation therapy (ADT) for nonmetastatic prostate cancer.
- **iv.** If the request is for Conexxence, Jubbonti, or Stoboclo, the member has experienced therapeutic failure or intolerance to plan-preferred Prolia.

b. The member is female and all of the following criteria are met **(i. through iv.)**:
- **i.** The member has a diagnosis of breast cancer (ICD-10: C50, D05).
- **ii.** The member has a T-score ≤ -1.0 and one (1) of the following criteria is met **(A) or B))**:
  - **A)** The member has multiple risk factors for a fracture.
  - **B)** The member has experienced a previous fragility fracture.
- **iii.** The member is receiving adjuvant aromatase therapy for breast cancer.
- **iv.** If the request is for Conexxence, Jubbonti, or Stoboclo, the member has experienced therapeutic failure or intolerance to plan-preferred Prolia.

2. Osteoporosis or Osteopenia (including Glucocorticoid-Induced Osteoporosis)

When a benefit, coverage of denosumab products for bone disease may be approved when all of the following criteria are met **(a. through d.)**:

a. The member is at high or very high risk for a fracture as defined by one (1) of the following criteria **(i., ii., or iii.)**:
- **i.** The member has a history of a previous hip (ICD-10: M84.359) or vertebral fracture (ICD-10: S22.0).
- **ii.** The member has a diagnosis of osteoporosis (ICD-10: M80-81) defined as a T-score ≤ -2.5.
- **iii.** The member has a diagnosis of osteopenia (no ICD-10 code) defined as a T-score between -1.0 and -2.5 and meets one (1) of the following criteria **(A), B), or C))**:
  - **A)** The 10-year risk of major osteoporotic fracture is ≥ 20% using the FRAX calculator.

B) The 10-year risk of hip fracture is ≥ 3% using the FRAX calculator.
C) The member meets both of the following criteria **(1) and 2))**:
1) The member is 40 years of age or older.
2) The member has a history of glucocorticoid use at a dose of 5 mg per day or more of prednisone (or equivalent) for at least 3 months.

b. The member has experienced therapeutic failure or intolerance to one (1) bisphosphonate or all bisphosphonates are contraindicated.
c. The member is not receiving Prolia in combination with other parathyroid hormone analogs, RANKL inhibitors, or sclerostin inhibitors.
d. If the request is for Conexxence, Jubbonti, or Stoboclo, the member has experienced therapeutic failure or intolerance to plan-preferred Prolia.

B. Evenity

1. Osteoporosis or Osteopenia
When a benefit, coverage of Evenity may be approved when all of the following criteria are met **(a. through e.)**:
a. The member is a postmenopausal female.
b. The member is at high or very high risk for a fracture as defined by one (1) of the following criteria **(i., ii., or iii.)**:
i. The member has a history of a previous hip (ICD-10: M84.359) or vertebral fracture (ICD-10: S22.0).
ii. The member has a diagnosis of osteoporosis (ICD-10: M80-81) defined as a T-score ≤ -2.5.
iii. The member has a diagnosis of osteopenia (no ICD-10 code) defined as a T-score between -1.0 and -2.5 and meets one (1) of the following criteria **(A) or B))**:
A) The 10-year risk of major osteoporotic fracture is ≥ 20% using the FRAX calculator.
B) The 10-year risk of hip fracture is ≥ 3% using the FRAX calculator.

c. The member meets one (1) of the following criteria **(i. or ii.)**:
i. The member has experienced therapeutic failure or intolerance to one (1) bisphosphonate or all bisphosphonates are contraindicated.
ii. The member is at very high risk for a fracture as defined by both of the following criteria **(A) and B))**:
A) The member has had multiple spine fractures.
B) The member has a T-score ≤ -2.5.

d. The member has not exceeded the lifetime limit of 12 monthly doses.
e. The member is not receiving Evenity in combination with other parathyroid hormone analogs, RANKL inhibitors, or sclerostin inhibitors.

II. An exception to some or all of the criteria above may be granted for select members and/or circumstances based on state and/or federal regulations.

Limitations of Coverage

I. Coverage of drugs addressed in this policy for disease states outside of the FDA-approved indications should be denied based on the lack of clinical data to support effectiveness and safety in other conditions unless otherwise noted in the approval criteria.
II. For Commercial or HCR members with a closed formulary, a non-formulary product will only be approved if the member meets the criteria for a formulary exception in addition to the criteria outlined within this policy.

Authorization Duration

- Commercial and HCR plans: If approved, up to a 12 month authorization may be granted.

Automatic Approval Criteria

None.

References:

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3. Jubbonti [package insert]. Princeton, NJ: Manufacturer Name; March 2024.
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9. North American Menopause Society. Position statement: management of osteoporosis in postmenopausal women: the 2021 position statement of The North American Menopause Society. *Menopause*. 2021; 28(9): 973-997.
10. Riggs BL, Khosla S, Melton 3rd LJ. Sex Steroids and the construction and conservation of the adult skeleton. *Endocr Rev.* 2002; 23:279-302.
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13. Amir Qaseem, Lauri A. Hicks, Itziar Etxeandia-Ikobaltzeta, et al; Clinical Guidelines Committee of the American College of Physicians. Pharmacologic Treatment of Primary Osteoporosis or Low Bone Mass to Prevent Fractures in Adults: A Living Clinical Guideline From the American College of Physicians. *Ann Intern Med*. 2023;176:224-238.