Corporate Medical Policy: Denosumab (Prolia®, Xgeva®) and Denosumab Biosimilars **"Notification"** **POLICY EFFECTIVE JANUARY 1, 2026**

Restricted Product(s):

- denosumab (Prolia®) subcutaneous injection for administration by a healthcare professional
- denosumab (Xgeva®) subcutaneous injection for administration by a healthcare professional
- denosumab-bbdz (Jubbonti®) subcutaneous injection for administration by a healthcare professional
- denosumab-bbdz (Wyost®) subcutaneous injection for administration by a healthcare professional
- denosumab-bmwo (Stoboclo®) subcutaneous injection for administration by a healthcare professional
- denosumab-bmwo (Osenvelt®) subcutaneous injection for administration by a healthcare professional
- denosumab-bnht (Conexxence®) subcutaneous injection for administration by a healthcare professional
- denosumab-bnht (Bomyntra®) subcutaneous injection for administration by a healthcare professional
- denosumab-dssb (Ospomyv®) subcutaneous injection for administration by a healthcare professional
- denosumab-dssb (Xbryk®) subcutaneous injection for administration by a healthcare professional
- denosumab-kyqq (Bosaya®) subcutaneous injection for administration by a healthcare professional
- denosumab-kyqq (Aukelso®) subcutaneous injection for administration by a healthcare professional
- denosumab-nxxp (Bildyos®) subcutaneous injection for administration by a healthcare professional
- denosumab-nxxp (Bilprevda®) subcutaneous injection for administration by a healthcare professional

FDA Approved Use:

- Denosumab (Prolia®), Denosumab-bbdz (Jubbonti®), Denosumab-bmwo (Stoboclo®), Denosumab-bnht (Conexxence®), Denosumab-dssb (Ospomyv®), Denosumab-kyqq (Bosaya®), Denosumab-nxxp (Bildyos®)
  - Treatment of postmenopausal women with osteoporosis at high risk for fracture
  - Treatment to increase bone mass in men with osteoporosis at high risk for fracture
  - Treatment of glucocorticoid-induced osteoporosis in men and women at high risk for fracture
  - 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

- Denosumab (Xgeva®), Denosumab-bbdz (Wyost®), Denosumab-bmwo (Osenvelt®), Denosumab-bnht (Bomyntra®), Denosumab-dssb (Xbryk®), Denosumab-kyqq (Aukelso®), Denosumab-nxxp (Bilprevda®)
  - Prevention of skeletal-related events in patients with multiple myeloma and in patients with bone metastases from solid tumors

- 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
- Treatment of hypercalcemia of malignancy refractory to bisphosphonate therapy

Criteria for Medical Necessity:

The restricted product(s) may be considered medically necessary when the following criteria are met:

1. The request is for **Prolia (denosumab)**, **Bildyos (denosumab-nxxp)**, **Bosaya (denosumab-kyqq)**, **Conexxence (denosumab-bnht)**, **Jubbonti (denosumab-bbdz)**, **Ospomyv (denosumab-dssb)**, or **Stoboclo (denosumab-bmwo)**; **AND**
    a. The patient is 18 years of age or older; **AND**
    b. The patient has a diagnosis of **osteoporosis**; **AND**
        i. ONE of the following:
            1. The patient is a male over 50 years old; **OR**
            2. The patient is a postmenopausal female; **AND**
        ii. The patient is at high risk for fracture defined by ONE of the following:
            1. History of osteoporotic fracture; **OR**
            2. Multiple risk factors for fracture; **AND**
        iii. ONE of the following:
            1. The patient has previously been treated with a bisphosphonate and experienced a therapeutic failure or inadequate response; **OR**
            2. The patient is unable to receive a bisphosphonate due to a contraindication/hypersensitivity; **OR**
    c. The patient has a diagnosis of **breast cancer**; **AND**
        i. The patient is currently receiving aromatase inhibitor therapy (e.g., anastrozole, letrozole, exemestane) for breast cancer; **AND**
        ii. ONE of the following:
            1. The patient has previously been treated with a bisphosphonate and experienced a therapeutic failure or inadequate response; **OR**
            2. The patient is unable to receive a bisphosphonate due to a contraindication/hypersensitivity; **OR**
    d. The patient has a diagnosis of **nonmetastatic prostate cancer**; **AND**
        i. The patient is currently receiving androgen deprivation therapy; **AND**
        ii. ONE of the following:

1. The patient has previously been treated with a bisphosphonate and experienced a therapeutic failure or inadequate response; **OR**
2. The patient is unable to receive a bisphosphonate due to a contraindication/hypersensitivity; **OR**

e. The patient has been diagnosed with **glucocorticoid-induced osteoporosis**; **AND**
   i. The patient is at high risk for fracture defined by ONE of the following:
      1. History of osteoporotic fracture; **OR**
      2. Multiple risk factors for fracture; **AND**
   ii. The patient is initiating or continuing systemic glucocorticoids in a daily dosage equal to 7.5 mg or greater of prednisone and expected to remain on therapy for at least 6 months; **AND**
   iii. ONE of the following:
      1. The patient has previously been treated with a bisphosphonate and experienced a therapeutic failure or inadequate response; **OR**
      2. The patient is unable to receive a bisphosphonate due to a contraindication/hypersensitivity; **AND**

f. If the request is for Prolia (denosumab), Bildyos (denosumab-nxxp), Bosaya (denosumab-kyqq), Conexxence (denosumab-bnht), Ospomyv (denosumab-dssb), or a non-preferred denosumab product, ONE of the following:
   i. The patient has tried and had an inadequate response to ALL of the following preferred denosumab biosimilar products: Jubbonti (denosumab-bbdz) AND Stoboclo (denosumab-bmwo) **[medical record documentation required]**; **OR**
   ii. The patient has an intolerance, FDA labeled contraindication, or hypersensitivity to Jubbonti (denosumab-bbdz) AND Stoboclo (denosumab-bmwo) that is NOT expected to occur with the requested agent **[medical record documentation required]**; **OR**
   iii. The patient has a documented serious adverse event that required medical intervention to Jubbonti (denosumab-bbdz) AND Stoboclo (denosumab-bmwo) that is NOT anticipated with the requested agent **[medical record documentation required]**; **AND**
      1. The prescriber has completed and submitted an FDA MedWatch Adverse Event Reporting Form **[medical record documentation required]**; **OR**

2. The request is for **Xgeva (denosumab)**, **Aukelso (denosumab-kyqq)**, **Bilprevda (denosumab-nxxp)**, **Bomyntra (denosumab-bnht)**, **Osenvelt (denosumab-bmwo)**, **Wyost (denosumab-bbdz)**, or **Xbryk (denosumab-dssb)**; **AND**
   a. The patient has a diagnosis of **multiple myeloma**; **AND**
      i. The requested agent will be used for prevention of skeletal-related events; **AND**
      ii. ONE of the following:
         1. The patient has had prior treatment with an intravenous bisphosphonate and experienced a therapeutic failure or inadequate response; **OR**

2. The patient has an intolerance, FDA labeled contraindication, or hypersensitivity to intravenous bisphosphonate therapy; **OR**

b. The patient has a **solid tumor cancer diagnosis** (e.g., thyroid, non-small cell lung, kidney cancer) AND has documented bone metastases; **AND**
   i. The requested agent will be used for prevention of skeletal-related events; **AND**
   ii. ONE of the following:
      1. The patient has had prior treatment with an intravenous bisphosphonate and experienced a therapeutic failure or inadequate response; **OR**
      2. The patient has an intolerance, FDA labeled contraindication, or hypersensitivity to intravenous bisphosphonate therapy; **OR**

c. The patient has a diagnosis of **giant cell tumor of bone**; **AND**
   i. The patient is an adult or skeletally mature adolescent (12 years of age or older); **AND**
   ii. ONE of the following:
      1. The tumor is recurrent; **OR**
      2. The tumor is unresectable; **OR**
      3. Surgical resection is likely to result in severe morbidity; **OR**

d. The patient has a diagnosis of **hypercalcemia of malignancy**; **AND**
   i. The patient has had prior treatment with an intravenous bisphosphonate and experienced a therapeutic failure or inadequate response; **OR**
   ii. The patient has an intolerance, FDA labeled contraindication, or hypersensitivity to intravenous bisphosphonate therapy; **OR**

e. The patient has a diagnosis of **breast cancer** AND has documented bone metastases; **AND**
   i. The patient has had prior treatment with an intravenous bisphosphonate and experienced a therapeutic failure or inadequate response; **OR**
   ii. The patient has an intolerance, FDA labeled contraindication, or hypersensitivity to intravenous bisphosphonate therapy; **OR**

f. The patient has a diagnosis of **castration-resistant prostate cancer** AND has documented bone metastases; **OR**

g. The patient has a diagnosis of **systemic mastocytosis**; **AND**
   i. The patient has had prior treatment with an intravenous bisphosphonate and experienced a therapeutic failure or inadequate response; **OR**
   ii. The patient has an intolerance, FDA labeled contraindication, or hypersensitivity to intravenous bisphosphonate therapy; **AND**

h. If the request is for Xgeva (denosumab), Aukelso (denosumab-kyqq), Bilprevda (denosumab-nxxp), Bomyntra (denosumab-bnht), Xbryk (denosumab-dssb), or a non-preferred denosumab product, ONE of the following:
   i. The patient has tried and had an inadequate response to ALL of the following preferred denosumab biosimilar products: Osenvelt (denosumab-bmwo) AND Wyost (denosumab-bbdz) **[medical record documentation required]**; **OR**

ii. The patient has an intolerance, FDA labeled contraindication, or hypersensitivity to Osenvelt (denosumab-bmwo) AND Wyost (denosumab-bbdz) that is NOT expected to occur with the requested agent **[medical record documentation required]**; **OR**
iii. The patient has a documented serious adverse event that required medical intervention to Osenvelt (denosumab-bmwo) AND Wyost (denosumab-bbdz) that is NOT anticipated with the requested agent **[medical record documentation required]**; **AND**
    1. The prescriber has completed and submitted an FDA MedWatch Adverse Event Reporting Form **[medical record documentation required]**; **AND**

3. The patient will NOT be using the requested agent in combination with a bisphosphonate, another form of denosumab (e.g., Prolia or Xgeva), romosozumab-aqqg, or a parathyroid hormone analog for osteoporosis (e.g., abaloparatide, teriparatide); **AND**
4. The requested quantity does NOT exceed the maximum units allowed for the duration of approval (see table below).

Duration of Approval: 365 days (1 year)

NOTE:
Use of Denosumab and Denosumab Biosimilars may be considered medically necessary for clinical indications not listed above when the drug is prescribed for the treatment of **cancer** either:

1. In accordance with FDA label (when clinical benefit has been established, and it is not determined to be investigational as defined in the Blue Cross NC Corporate Medical Policy (CMP), "Investigational (Experimental) Services." [please refer to CMP "Investigational (Experimental) Services" for a summary of evidence standards from nationally recognized compendia]; **OR**
2. In accordance with specific strong endorsement or support by nationally recognized compendia, when such recommendation is based on strong/high levels of evidence, and/or uniform consensus of clinical appropriateness has been reached.

FDA Label Reference				
Medication	**Indication**	**Dosing**	**HCPCS**	**Maximum Units***
denosumab (Prolia®) subcutaneous (SC) injection	Postmenopausal osteoporosis in women at high risk for fracture	60 mg SC every 6 months	J0897	120
denosumab-bbdz (Jubbonti®) subcutaneous (SC) injection			Q5136	

FDA Label Reference				
Medication	**Indication**	**Dosing**	**HCPCS**	**Maximum Units***
denosumab-bmwo (Stoboclo®) subcutaneous (SC) injection	Osteoporosis in men at high risk for fracture, to increase bone mass		Q5157	
denosumab-bnht (Conexxence®) subcutaneous (SC) injection	Glucocorticoid-induced osteoporosis in men and women at high risk for fracture		Q5158	
denosumab-dssb (Ospomyv®) subcutaneous (SC) injection	To increase bone mass in men at high risk for fracture receiving androgen deprivation therapy for nonmetastatic prostate cancer		Q5159	
denosumab-kyqq (Bosaya®) subcutaneous (SC) injection	To increase bone mass in women at high risk for fracture receiving adjuvant aromatase inhibitor therapy for breast cancer		C9399** J3490** J3590**	
denosumab-nxxp (Bildyos®) subcutaneous (SC) injection			C9399** J3490** J3590**	
denosumab (Xgeva®) subcutaneous (SC) injection	Prevention of skeletal-related events in patients with multiple myeloma and in patients with bone metastases from solid tumors Giant cell tumor of bone that is unresectable or where surgical resection is likely to result in severe morbidity, in adults and skeletally mature adolescents Hypercalcemia of malignancy refractory to bisphosphonate therapy	Multiple myeloma and bone metastasis from solid tumors: 120 mg SC every 4 weeks Giant cell tumor of bone: 120 mg SC every 4 weeks with additional 120 mg doses on Days 8 and 15 of the first month of therapy Hypercalcemia of malignancy: 120 mg SC every 4 weeks with additional 120 mg doses on	J0897	Multiple myeloma: 1,560 Giant cell tumor of bone: 1,800 Hypercalcemia of malignancy: 1,800
denosumab-bbdz (Wyost®) subcutaneous (SC) injection			Q5136	
denosumab-bmwo (Osenvelt®) subcutaneous (SC) injection			Q5157	
denosumab-bnht (Bomyntra®) subcutaneous (SC) injection			Q5158	
denosumab-dssb (Xbryk®) subcutaneous (SC) injection			Q5159	

FDA Label Reference				
Medication	**Indication**	**Dosing**	**HCPCS**	**Maximum Units***
denosumab-kyqq (Aukelso®) subcutaneous (SC) injection		Days 8 and 15 of the first month of therapy	C9399** J3490** J3590** J9999**	
denosumab-nxxp (Bilprevda®) subcutaneous (SC) injection			C9399** J3490** J3590** J9999**	

***Maximum units allowed for duration of approval**
****Non-specific assigned HCPCS codes, must submit requested product NDC**

Other applicable codes may include:

ICD-10 Codes: C00.0-C49.9, C4A.0-C4A.9, C50.011-C79.9, C7A.00-C7A.8, C7B.00-C7B.8, C80.0- C86.6, C88.2-C96.Z, D00.00-D09.9, M81.0, M81.8, T50.905, Z51.11, Z51.12, Z79.811, Z87.311
For oncology use, the cancer diagnosis code must also be included when the following codes are used: M81.0, M81.8, T50.905, Z79.811, Z87.311

References: all information referenced is from FDA package insert unless otherwise noted below.

1. Ellis GK, Bone HG, Chlebowski R, et al. Randomized trial of denosumab in patients receiving adjuvant aromatase inhibitors for nonmetastatic breast cancer. 2008 Oct;26:4875-4882.
2. McClung MR, Lewiecki EM, Cohen SB, et al. Denosumab in postmenopausal women with low bone mineral density. *N Engl J Med*. 2006; 354:821-831.
3. North American Menopause Society (NAMS). Management of osteoporosis in postmenopausal women: 2010 position statement of The North American Menopause Society. *Menopause*. 2010:17(1):25-54.

Policy Implementation/Update Information: Criteria and treatment protocols are reviewed annually by the Blue Cross NC P&T Committee, regardless of change. This policy is reviewed in Q1 annually.

January 2026: Criteria change: Added new to market Prolia (denosumab) biosimilars Bildyos (denosumab-nxxp) and Bosaya (denosumab-kyqq) to policy for the same FDA approved indications as Prolia and with the same coverage criteria requirements. For Prolia, Bildyos,

Bosaya, Conexxence, and Ospomyv: added additional corresponding criteria as a non-preferred denosumab product with requirement of trial and failure of both Jubbonti AND Stoboclo (preferred denosumab biosimilar products), or presence of a documented serious adverse event requiring medical intervention from both preferred denosumab biosimilar products that is not anticipated with the requested non-preferred denosumab product, with required submission of an FDA MedWatch Adverse Event Reporting Form. Added new to market Xgeva (denosumab) biosimilars Aukelso (denosumab-kyqq) and Bilprevda (denosumab-nxxp) to policy for the same FDA approved indications as Xgeva and with the same coverage criteria requirements. For Xgeva, Aukelso, Bilprevda, Bomyntra, and Xbryk: added additional corresponding criteria as a non-preferred denosumab product with requirement of trial and failure of both Osenvelt AND Wyost (preferred denosumab biosimilar products), or presence of a documented serious adverse event requiring medical intervention from both preferred denosumab biosimilar products that is not anticipated with the requested non-preferred denosumab product, with required submission of an FDA MedWatch Adverse Event Reporting Form. For Xgeva and Xgeva biosimilar products: added requirement of trial and failure of an IV bisphosphonate to multiple myeloma and solid tumor with bone metastases indications; added indication for breast cancer with bone metastases with requirement of trial and failure of an IV bisphosphonate; added indication for castration-resistant prostate cancer with bone metastases; added indication for systemic mastocytosis with requirement of trial and failure of an IV bisphosphonate. For all restricted products and indications, added requirement of no use in combination with a bisphosphonate, another form of denosumab (e.g., Prolia or Xgeva), romosozumab-aqqg, or a parathyroid hormone analog for osteoporosis. Adjusted maximum units for oncologic indications according to FDA labeled dosing. Consolidated FDA label reference table for clarity. Other minor formatting adjustments made throughout policy for clarity. **Policy notification given 10/1/2025 for effective date 1/1/2026**.

October 2025: Coding change: For denosumab-bmwo (Stoboclo/Osenvelt), added HCPCS code Q5157 (1 unit per 1 mg) to dosing reference table effective 10/1/2025; deleted C9399, J3490, J3590, and J9999 termed 9/30/2025. For denosumab-bnht (Bomyntra/Conexxence), added HCPCS code Q5158 (1 unit per 1 mg) to dosing reference table effective 10/1/2025; deleted C9399, J3490, J3590, and J9999 termed 9/30/2025. For denosumab-dssb (Ospomyv/Xbryk), added HCPCS code Q5159 (1 unit per 1 mg) to dosing reference table effective 10/1/2025; deleted C9399, J3490, J3590, and J9999 termed 9/30/2025.

October 2025: Criteria change: For Conexxence, Jubbonti, Ospomyv, and Stoboclo, removed requirement of trial and failure of Prolia. For Bomyntra, Osenvelt, Wyost, and Xbryk, removed requirement of trial and failure of Xgeva.

June 2025: Criteria change: Added new to market Prolia (denosumab) biosimilars Conexxence (denosumab-bnht), Jubbonti (denosumab-bbdz), Ospomyv (denosumab-dssb), and Stoboclo (denosumab-bmwo) to policy for the same FDA approved indications as Prolia and with the same coverage criteria requirements. For Conexxence, Jubbonti, Ospomyv, and Stoboclo, added additional corresponding criteria as a non-preferred Prolia (denosumab) biosimilar product with requirement of trial and failure of Prolia. Added new to market Xgeva (denosumab) biosimilars Bomyntra (denosumab-bnht), Osenvelt (denosumab-bmwo), Wyost (denosumab-bbdz), and Xbryk (denosumab-dssb) to policy for the same FDA approved indications as Xgeva and with the same coverage criteria requirements. For Bomyntra, Osenvelt, Wyost, and Xbryk, added additional corresponding criteria as a non-preferred Xgeva (denosumab) biosimilar product with requirement of trial and failure of Xgeva. Added associated dosing, maximum units, and HCPCS codes (Q5136 [Jubbonti/Wyost], C9399, J3490, and J3590 [for Conexxence, Ospomyv, and Stoboclo], C9399, J3490, J3590, and J9999 [for Bomyntra, Osenvelt, and Xbryk]) to FDA label reference table. Changed policy name to “Denosumab (Prolia®, Xgeva®) and Denosumab Biosimilars” from “Denosumab (Prolia®, Xgeva®)”. Adjusted

maximum units for oncology indications to 9999 to indicate unlimited units for clarity. Other minor adjustments made to formatting of FDA label reference table for clarity with no change to intent.
June 2021: Criteria change: Added trial and failure or contraindication /hypersensitivity to a bisphosphonate for patients with breast cancer or prostate cancer at high risk for fracture; added maximum units; medical policy formatting change. **Policy notification given 4/16/2021 for effective date 6/16/2021**.
*Further historical criteria changes and updates available upon request from Medical Policy and/or Corporate Pharmacy.