Clinical Policy: Denosumab (Prolia, Xgeva), Denosumab-bbdz (Jubbonti, Wyost), Denosumab-dssb (Ospomyv, Xbryk), Denosumab-bmwo (Stoboclo, Osenvelt), Denosumab-bnht (Bomyntra, Conexxence), Denosumab-nxxp (Bildyos, Bilprevda), Denosumab-kyqq (Bosaya, Aukelso), Denosumab- qbde (Enoby, Xtrenbo), Denosumab-desu (Osvyrti, Jubereq), Denosumab-mobz (Boncresa, Oziltus), Denosumab-adet (Ponlimsi, Degevma)

Reference Number: CP.PHAR.58
Effective Date: 03.01.11
Last Review Date: 08.26
Line of Business: Medicaid

Coding Implications
Revision Log

See Important Reminder at the end of this policy for important regulatory and legal information.

Description

Denosumab (Prolia®, Xgeva®) and its biosimilars, denosumab-bbdz (Jubbonti®, Wyost®), denosumab-bmwo (Stoboclo®, Osenvelt®), denosumab-bnht (Bomyntra®, Conexxence®), denosumab-dssb (Ospomyv™, Xbryk™), denosumab-nxxp (Bildyos®, Bilprevda®), denosumab-kyqq (Bosaya™, Aukelso™), denosumab-qbde (Enoby™, Xtrenbo™), denosumab-desu (Osvyrti®, Jubereq®), denosumab-mobz (Boncresa®, Oziltus®), and denosumab-adet (Ponlimsi™, Degevma™), are receptor activators of nuclear factor kappa-B ligand inhibitor.

FDA Approved Indication(s)

Prolia, Bildyos, Boncresa, Bosaya, Conexxence, Enoby, Jubbonti, Ospomyv, Osvyrti, Ponlimsi, Stoboclo, denosumab-bnht, and denosumab-dssb are indicated:

- For the treatment of postmenopausal women with osteoporosis (PMO) at high risk for fracture*, or patients who have failed or are intolerant to other available osteoporosis therapy. In postmenopausal women with osteoporosis, denosumab reduces the incidences of vertebral, nonvertebral, and hip fractures.
- For the treatment to increase bone mass in men with osteoporosis at high risk for fracture*, or patients who have failed or are intolerant to other available osteoporosis therapy.
- For the treatment of glucocorticoid-induced osteoporosis (GIO) 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 of prednisone and expected to remain on glucocorticoids for ≥ 6 months.
- For treatment to increase bone mass in men at high risk for fracture* receiving androgen deprivation therapy (ADT) for nonmetastatic prostate cancer. In these patients denosumab also reduced the incidence of vertebral fractures.
- For treatment to increase bone mass in women at high risk for fracture* receiving adjuvant aromatase inhibitor therapy for breast cancer.

**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.*

Xgeva, Aukelso, Bilprevda, Bomyntra, Degevma, Jubereq, Osenvelt, Oziltus, Wyost, Xbryk, Xtrenbo, and denosumab-bnht are indicated:

- For the prevention of skeletal-related events in patients with multiple myeloma (MM) and in patients with bone metastases from solid tumors.
- 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.
- For the treatment of hypercalcemia of malignancy refractory to bisphosphonate therapy.

Policy/Criteria
Provider must submit documentation (such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria.

Index

I. Initial Approval Criteria
- **A.** Osteoporosis *(Prolia, Bildyos, Boncresa, Bosaya, Conexxence, Enoby, Jubbonti, Ospomyv, Osvyrti, Ponlimsi, Stoboclo, denosumab-bnht, or denosumab-dssb)*
- **B.** Prostate/Breast Cancer - Fracture Prevention *(Prolia, Bildyos, Boncresa, Bosaya, Conexxence, Enoby, Jubbonti, Ospomyv, Osvyrti, Ponlimsi, Stoboclo, denosumab-bnht, or denosumab-dssb)*
- **C.** Multiple Myeloma or Solid Tumor *(Xgeva, Aukelso, Bilprevda, Bomyntra, Degevma, Jubereq, Osenvelt, Oziltus, Wyost, Xbryk, Xtrenbo, or denosumab-bnht)*
- **D.** Giant Cell Tumor of Bone *(Xgeva, Aukelso, Bilprevda, Bomyntra, Degevma, Jubereq, Osenvelt, Oziltus, Wyost, Xbryk, Xtrenbo, or denosumab-bnht)*
- **E.** Hypercalcemia of Malignancy *(Xgeva, Aukelso, Bilprevda, Bomyntra, Degevma, Jubereq, Osenvelt, Oziltus, Wyost, Xbryk, Xtrenbo, or denosumab-bnht)*
- **F.** Systemic Mastocytosis (off-label) *(Xgeva, Aukelso, Bilprevda, Bomyntra, Degevma, Jubereq, Osenvelt, Oziltus, Wyost, Xbryk, Xtrenbo, or denosumab-bnht)*
- **G.** Other diagnoses/indications

II. Continued Therapy
- **A.** All Indications in Section I *(Prolia, Bildyos, Boncresa, Bosaya, Conexxence, Degevma, Enoby, Jubbonti, Ospomyv, Osvyrti, Ponlimsi, Stoboclo, Xgeva, Aukelso, Bilprevda, Bomyntra, Jubereq, Osenvelt, Oziltus, Wyost, Xbryk, Xtrenbo, denosumab-bnht, or denosumab-dssb)*
- **B.** Other diagnoses/indications

III. Diagnoses/Indications for which coverage is NOT authorized
IV. Appendices/General Information
V. Dosage and Administration
VI. Product Availability
VII. References

It is the policy of health plans affiliated with Centene Corporation® that Aukelso, Bildyos, Boncresa, Bilprevda, Bomyntra, Bosaya, Conexxence, Degevma, Enoby, Jubereq, Jubbonti, Osenvelt, Ospomyv, Osvyrti, Oziltus, Ponlimsi, Prolia, Stoboclo, Wyost, Xbryk, Xgeva, Xtrenbo, denosumab-bnht, and denosumab-dssb are **medically necessary** when the following criteria are met:

I. Initial Approval Criteria

A. Osteoporosis (must meet all)**:**

1. Request is for Prolia, Bildyos, Boncresa, Bosaya, Conexxence, Enoby, Jubbonti, Ospomyv, Osvyrti, Ponlimsi, Stoboclo, denosumab-bnht, or denosumab-dssb;
2. Diagnosis of PMO, GIO, or male osteoporosis and one of the following (a or b):
   a. Member is at very high risk for fracture as evidenced by one of the following (i, ii, or iii):
      i. Recent osteoporotic fracture (within the past 12 months);
      ii. Bone mineral density (BMD) T-score at hip or spine ≤ -3.0 *(see Appendix F)*;
      iii. BMD T-score at hip or spine ≤ -2.5 AND major osteoporotic fracture (i.e., hip, spine, forearm, wrist, humerus) *(see Appendix F)*;
   b. Member has completed a 3-year trial of bisphosphonate therapy* *(see Appendix B; generic alendronate is preferred)* at up to maximally indicated doses unless one of the following (i-v):
      i. All bisphosphonates are contraindicated;
      ii. Clinically significant adverse effects are experienced to both IV and PO formulations (*see Appendix D*);
      iii. Member has experienced a loss of BMD while receiving bisphosphonate therapy;
      iv. Member has experienced a lack of BMD increase after ≥ 12 months of bisphosphonate therapy;
      v. Member experienced an osteoporotic fracture or fragility fracture while receiving bisphosphonate therapy;

   **Prior authorization may be required for bisphosonates.*
3. Age ≥ 18 years or documentation of closed epiphyses on x-ray;
4. If request is for a product other than Bildyos and Enoby, member must use Bildyos and Enoby, unless clinically significant adverse effects are experienced or both are contraindicated;
5. Prolia, Bildyos, Boncresa, Bosaya, Conexxence, Enoby, Jubbonti, Ospomyv, Osvyrti, Ponlimsi, Stoboclo, denosumab-bnht, or denosumab-dssb are not prescribed concurrently with Xgeva, Aukelso, Bilprevda, Bomyntra, Degevma, Jubereq, Osenvelt, Oziltus, Wyost, Xbryk, or Xtrenbo;
6. Dose does not exceed 60 mg every 6 months.

Approval duration: 12 months

B. Prostate/Breast Cancer - Fracture Prevention (must meet all)**:**

1. Request is for Prolia, Bildyos, Boncresa, Bosaya, Conexxence, Enoby, Jubbonti, Ospomyv, Osvyrti, Ponlimsi, Stoboclo, denosumab-bnht, or denosumab-dssb;
2. Diagnosis of one of the following (a or b):
   a. Prostate cancer, and member is receiving ADT (e.g., leuprolide (Lupron®), bicalutamide (Casodex®) or nilutamide (Nilandron®));
   b. Breast cancer, and member is receiving adjuvant endocrine therapy (e.g., tamoxifen or aromatase inhibitors such as anastrozole (Arimidex®), exemestane (Aromasin®) or letrozole (Femara®));
3. Member does not have bone metastasis;
4. Prescribed by or in consultation with an oncologist;

5. Age ≥ 18 years or documentation of closed epiphyses on x-ray;
6. Member meets one of the following (a, b, or c):*
   a. For breast cancer, failure of zoledronic acid* (formerly Zometa) or pamidronate*, at up to maximally indicated doses unless clinically significant adverse effects are experienced or both are contraindicated *(see Appendices B and D)*;
      **Prior authorization may be required.*
   b. For prostate cancer, failure of zoledronic acid* (formerly Zometa) at up to maximally indicated doses unless contraindicated or clinically significant adverse effects are experienced *(see Appendices B and D)*;
      **Prior authorization may be required.*
   c. Request is for the treatment associated with cancer for a State with regulations against step therapy in certain oncology settings (*see Appendix E*);
7. If request is for a product other than Bildyos and Enoby, member must use Bildyos and Enoby, unless clinically significant adverse effects are experienced or both are contraindicated;
8. Prolia, Bildyos, Boncresa, Bosaya, Conexxence, Enoby, Jubbonti, Ospomyv, Osvyrti, Ponlimsi, Stoboclo, denosumab-bnht, or denosumab-dssb are not prescribed concurrently with Xgeva, Aukelso, Bilprevda, Bomyntra, Degevma, Jubereq, Osenvelt, Oziltus, Wyost, Xbryk, or Xtrenbo;
9. Dose does not exceed 60 mg every 6 months.

Approval duration: 12 months

C. Multiple Myeloma or Solid Tumor (must meet all)**:**
1. Request is for Xgeva, Aukelso, Bilprevda, Bomyntra, Degevma, Jubereq, Osenvelt, Oziltus, Wyost, Xbryk, Xtrenbo, or denosumab-bnht;
2. Diagnosis of one of the following (a or b):
   a. MM;
   b. Bone metastasis secondary to solid tumor (e.g., breast, kidney, lung, prostate, thyroid);
3. Prescribed by or in consultation with an oncologist;
4. Age ≥ 18 years or documentation of closed epiphyses on x-ray;
5. For indications other than prostate or breast cancer, member meets one of the following (a or b):*
   a. Failure of zoledronic acid* (formerly Zometa) or pamidronate* at up to maximally indicated doses, unless clinically significant adverse effects are experienced or both are contraindicated (*see Appendices B and D*);
      **Prior authorization may be required.*
   b. Request is for the treatment associated with cancer for a State with regulations against step therapy in certain oncology settings (*see Appendix E*);
6. If request is for a product other than Bilprevda and Xtrenbo, member must use Bilprevda and Xtrenbo, unless clinically significant adverse effects are experienced, both are contraindicated, or request is for treatment associated with cancer for a State with regulations against step therapy in certain oncology settings *(see Appendix E)*;*
7. Xgeva, Aukelso, Bilprevda, Bomyntra, Degevma, Jubereq, Osenvelt, Oziltus, Wyost, Xbryk, Xtrenbo, or denosumab-bnht are not prescribed concurrently with Prolia, Bildyos, Boncresa, Bosaya, Conexxence, Enoby, Jubbonti, Ospomyv, Osvyrti, Ponlimsi, Stoboclo, or denosumab-dssb;

8. Dose does not exceed 120 mg every 4 weeks.

Approval duration: 12 months

D. Giant Cell Tumor of Bone (must meet all)**:**
1. Request is for Xgeva, Aukelso, Bilprevda, Bomyntra, Degevma, Jubereq, Osenvelt, Oziltus, Wyost, Xbryk, Xtrenbo, or denosumab-bnht;
2. Diagnosis of giant cell tumor of bone that is characterized as one of the following (a, b, or c):
   a. Metastatic or unresectable disease;
   b. Localized disease, and Xgeva, Aukelso, Bilprevda, Bomyntra, Degevma, Jubereq, Osenvelt, Oziltus, Wyost, Xbryk, Xtrenbo, or denosumab-bnht are prescribed as a single agent or in combination with serial embolization and/or radiation therapy;
   c. Resectable disease where surgical resection is likely to result in severe morbidity;
3. Prescribed by or in consultation with an oncologist;
4. Age ≥ 18 years or documentation of closed epiphyses on x-ray;
5. If request is for a product other than Bilprevda and Xtrenbo, member must use Bilprevda and Xtrenbo, unless clinically significant adverse effects are experienced, both are contraindicated, or request is for treatment associated with cancer for a State with regulations against step therapy in certain oncology settings *(see Appendix E)*;*
6. Xgeva, Aukelso, Bilprevda, Bomyntra, Degevma, Jubereq, Osenvelt, Oziltus, Wyost, Xbryk, Xtrenbo, or denosumab-bnht are not prescribed concurrently with Prolia, Bildyos, Boncresa, Bosaya, Conexxence, Enoby, Jubbonti, Ospomyv, Osvyrti, Ponlimsi, Stoboclo, or denosumab-dssb;
7. Dose does not exceed 120 mg every 4 weeks plus 120 mg on days 8 and 15 of first month of therapy.

Approval duration: 12 months

E. Hypercalcemia of Malignancy (must meet all)**:**
1. Request is for Xgeva, Aukelso, Bilprevda, Bomyntra, Degevma, Jubereq, Osenvelt, Oziltus, Wyost, Xbryk, Xtrenbo, or denosumab-bnht;
2. Diagnosis of hypercalcemia of malignancy:
3. Prescribed by or in consultation with an oncologist;
4. Age ≥ 18 years or documentation of closed epiphyses on x-ray;
5. Albumin-corrected calcium > 12.5 mg/dL despite IV bisphosphonate therapy in the last 30 days (*see Appendix B*);
   **Prior authorization may be required.*
6. If request is for a product other than Bilprevda and Xtrenbo, member must use Bilprevda and Xtrenbo, unless clinically significant adverse effects are experienced, both are contraindicated, or request is for treatment associated with cancer for a State with regulations against step therapy in certain oncology settings *(see Appendix E)*;*
7. Xgeva, Aukelso, Bilprevda, Bomyntra, Degevma, Jubereq, Osenvelt, Oziltus, Wyost, Xbryk, Xtrenbo, or denosumab-bnht are not prescribed concurrently with Prolia, Bildyos, Boncresa, Bosaya, Conexxence, Enoby, Jubbonti, Ospomyv, Osvyrti, Ponlimsi, Stoboclo, or denosumab-dssb;
8. Dose does not exceed 120 mg every 4 weeks plus 120 mg on days 8 and 15 of first month of therapy.

Approval duration: 12 months

F. Systemic Mastocytosis (off-label) (must meet all)**:**
1. Request is for Xgeva, Aukelso, Bilprevda, Bomyntra, Degevma, Jubereq, Osenvelt, Oziltus, Wyost, Xbryk, Xtrenbo, or denosumab-bnht;
2. Diagnosis of systemic mastocytosis;
3. Member has osteopenia or osteoporosis with bone pain;
4. Prescribed by or in consultation with an oncologist;
5. Age ≥ 18 years or documentation of closed epiphyses on x-ray;
6. Member meets one of the following (a or b):
   a. Failure of zoledronic acid* (formerly Zometa) or pamidronate* at up to maximally indicated doses unless clinically significant adverse effects are experienced or both are contraindicated *(see Appendices B and D)*;
   **Prior authorization may be required.*
   b. Request is for the treatment associated with cancer for a State with regulations against step therapy in certain oncology settings (*see Appendix E*);
7. If request is for a product other than Bilprevda and Xtrenbo, member must use Bilprevda and Xtrenbo, unless clinically significant adverse effects are experienced, both are contraindicated, or request is for treatment associated with cancer for a State with regulations against step therapy in certain oncology settings *(see Appendix E)*;*
8. Xgeva, Aukelso, Bilprevda, Bomyntra, Degevma, Jubereq, Osenvelt, Oziltus, Wyost, Xbryk, Xtrenbo, or denosumab-bnht are not prescribed concurrently with Prolia, Bildyos, Boncresa, Bosaya, Conexxence, Enoby, Jubbonti, Ospomyv, Osvyrti, Ponlimsi, Stoboclo, or denosumab-dssb;
9. Dose is within FDA maximum limit for any FDA-approved indication or is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (prescriber must submit supporting evidence).*
   **Prescribed regimen must be FDA-approved or recommended by NCCN.*

Approval duration: 12 months

G. Other diagnoses/indications (must meet 1 or 2)**:**
1. If this drug has recently (within the last 6 months) undergone a label change (e.g., newly approved indication, age expansion, new dosing regimen) that is not yet reflected in this policy, refer to one of the following policies (a or b):
   a. For drugs on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the no coverage criteria policy for the relevant line of business: CP.PMN.255 for Medicaid; or
   b. For drugs NOT on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the non-formulary policy for the relevant line of business: CP.PMN.16 for Medicaid; or
2. If the requested use (e.g., diagnosis, age, dosing regimen) is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized) AND criterion 1 above does not apply, refer to the off-label use policy for the relevant line of business: CP.PMN.53 for Medicaid.

II. Continued Therapy

A. All Indications in Section I (must meet all)**:**

1. Member meets one of the following (a, b, or c):
   a. Currently receiving medication via Centene benefit or member has previously met initial approval criteria;
   b. Member is currently receiving medication and is enrolled in a state and product with continuity of care regulations (*refer to state specific addendums for CC.PHARM.03A and CC.PHARM.03B);*
   c. Documentation supports that member is currently receiving Prolia, Xgeva, Aukelso, Bildyos, Boncresa, Bosaya, Conexxence, Degevma, Enoby, Jubbonti, Wyost, Bilprevda, Bomyntra, Ospomyv, Xbryk, Jubereq, Osenvelt, Osvyrti, Oziltus, Ponlimsi, Stoboclo, Xtrenbo, denosumab-bnht, or denosumab-dssb for a covered cancer-related indication and has received this medication for at least 30 days;
2. Member is responding positively to therapy;
3. If request is for a product other than Bilprevda and Xtrenbo in one of the following conditions (a – e), member must use Bilprevda and Xtrenbo, unless clinically significant adverse effects are experienced, both are contraindicated, or request is for treatment associated with cancer for a State with regulations against step therapy in certain oncology settings *(see Appendix E*):*
   a. Multiple myeloma;
   b. Bone metastasis secondary to solid tumor;
   c. Giant cell tumor of the bone;
   d. Hypercalcemia of malignancy;
   e. Systemic mastocytosis;
4. If request is for a product other than Bildyos and Enoby in one of the following conditions (a or b), member must use Bildyos and Enoby, unless clinically significant adverse effects are experienced or both are contraindicated:
   a. Osteoporosis;
   b. Fracture prevention in prostate or breast cancer;
5. If request is for a dose increase, new dose does not exceed (a or b):
   a. Prolia, Bildyos, Boncresa, Bosaya, Conexxence, Enoby, Jubbonti, Ospomyv, Osvyrti, Ponlimsi, Stoboclo, denosumab-bnht, or denosumab-dssb: 60 mg every 6 months;
   b. Xgeva, Aukelso, Bilprevda, Bomyntra, Degevma, Jubereq, Osenvelt, Oziltus, Wyost, Xbryk, Xtrenbo, or denosumab-bnht: 120 mg every 4 weeks or is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (prescriber must submit supporting evidence).*

**Prescribed regimen must be FDA-approved or recommended by NCCN.*

Approval duration: 12 months

B. Other diagnoses/indications (must meet 1 or 2)**:**

1. If this drug has recently (within the last 6 months) undergone a label change (e.g., newly approved indication, age expansion, new dosing regimen) that is not yet reflected in this policy, refer to one of the following policies (a or b):
   a. For drugs on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the no coverage criteria policy for the relevant line of business: CP.PMN.255 for Medicaid; or

b. For drugs NOT on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the non-formulary policy for the relevant line of business: CP.PMN.16 for Medicaid; or

2. If the requested use (e.g., diagnosis, age, dosing regimen) is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized) AND criterion 1 above does not apply, refer to the off-label use policy for the relevant line of business: CP.PMN.53 for Medicaid.

III. Diagnoses/Indications for which coverage is NOT authorized:

A. Non-FDA approved indications, which are not addressed in this policy, unless there is sufficient documentation of efficacy and safety according to the off label use policies – CP.PMN.53 for Medicaid or evidence of coverage documents.

IV. Appendices/General Information

Appendix A: Abbreviation/Acronym Key

ADT: androgen deprivation therapy
BMD: bone mineral density
CKD-MBD: chronic kidney disease-mineral bone disorder
FDA: Food and Drug Administration
GIO: glucocorticoid-induced osteoporosis
MM: multiple myeloma
PMO: postmenopausal osteoporosis

Appendix B: Therapeutic Alternatives

This table provides a listing of preferred alternative therapy recommended in the approval criteria. The drugs listed here may not be a formulary agent for all relevant lines of business and may require prior authorization.

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
IV bisphosphonates		
ibandronate (Boniva®)	Treatment: PMO Hypercalcemia of malignancy (*off-label)*	Varies *See prescribing information and compendia for dosing.*
zoledronic acid (Reclast®; formerly Zometa®)	<u>Reclast:</u> Treatment/prevention: PMO, GIO Treatment: male osteoporosis <u>Zometa:</u> MM Bone metastasis from solid tumors Hypercalcemia of malignancy Systemic mastocytosis *(off-label)* Fracture prevention - breast/prostate cancer (*off-label*)	
pamidronate	MM Bone metastasis from breast cancer Hypercalcemia of malignancy Systemic mastocytosis *(off-label)* Fracture prevention – breast/prostate cancer (*off-label*)	

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
Oral bisphosphonates		
alendronate (Fosamax®)	Treatment: PMO Treatment: GIO, male osteoporosis	Varies *See prescribing information and compendia for dosing.*
Fosamax® Plus D (alendronate / cholecalciferol)	Treatment: PMO, male osteoporosis	
risedronate (Actonel®, Atelvia®)	Actonel: Treatment: PMO, GIO Treatment: male osteoporosis Atelvia: Treatment: PMO	
ibandronate (Boniva®)	Treatment/prevention: PMO	

Therapeutic alternatives are listed as Brand name® (generic) when the drug is available by brand name only and generic (Brand name®) when the drug is available by both brand and generic.

Appendix C: Contraindications/Boxed Warnings

- Contraindication(s):
  - Prolia, Bildyos, Boncresa, Bosaya, Conexxence, Enoby, Jubbonti, Ospomyv, Osvyrti, Ponlimsi, Stoboclo, denosumab-bnht, and denosumab-dssb: hypocalcemia, pregnancy, known hypersensitivity to denosumab products
  - Xgeva, Aukelso, Bilprevda, Bomyntra, Degevma, Jubereq, Osenvelt, Oziltus, Wyost, Xbryk, Xtrenbo, and denosumab-bnht: hypocalcemia, known clinically significant hypersensitivity to denosumab products
- Boxed warning(s):
  - Xgeva, Aukelso, Bilprevda, Bomyntra, Degevma, Jubereq, Osenvelt, Oziltus, Wyost, Xbryk, Xtrenbo, and denosumab-bnht: none reported
  - Prolia, Bildyos, Boncresa, Bosaya, Conexxence, Enoby, Jubbonti, Ospomyv, Osvyrti, Ponlimsi, Stoboclo, denosumab-bnht, and denosumab-dssb:
    - Patients with advanced chronic kidney disease are at greater risk of severe hypocalcemia following Prolia, Bildyos, Boncresa, Bosaya, Conexxence, Enoby, Jubbonti, Ospomyv, Osvyrti, Ponlimsi, Stoboclo, and denosumab-dssb administration. Severe hypocalcemia resulting in hospitalization, life-threatening events and fatal cases have been reported.
    - The presence of chronic kidney disease-mineral bone disorder (CKD-MBD) markedly increases the risk of hypocalcemia.
    - Prior to initiating Prolia, Bildyos, Boncresa, Bosaya, Conexxence, Enoby, Jubbonti, Ospomyv, Osvyrti, Ponlimsi, Stoboclo, denosumab-bnht, and denosumab-dssb in patients with advanced chronic kidney disease, evaluate for the presence of CKD-MBD. Treatment with Prolia, Bildyos, Boncresa, Bosaya, Conexxence, Enoby, Jubbonti, Ospomyv, Osvyrti, Ponlimsi, Stoboclo, denosumab-bnht, and denosumab-dssb in these patients should be supervised by a healthcare provider with expertise in the diagnosis and management of CKD-MBD.

Appendix D: IV/PO Bisphosphonates: Examples of Contraindications and Adverse Effects

Bisphosphonates	Oral Formulations	IV Formulations
Contraindications		
Hypocalcemia	X	X
Increased risk of aspiration	X	-
Hypersensitivity to product component	X	X
Inability to stand/sit upright for at least 30 minutes	X	-
Creatinine clearance < 35 mL/min or evidence of acute renal impairment	-	X
Esophagus abnormalities which delay emptying such as stricture or achalasia	X	-
Clinically significant warnings or adverse side effects		
Pregnancy	X	X
Eye inflammation	X	X
Acute renal failure	X	X
Osteonecrosis of the jaw	X	X
Atypical femoral shaft fracture	X	X
Drug interactions (product-specific)	X	X
Severe or incapacitating musculoskeletal pain	X	X

Appendix E: States with Regulations against Redirections in Stage III, IV or Metastatic Cancer

State	Step Therapy Prohibited?	Notes
FL	Yes	For stage 4 metastatic cancer and associated conditions.
GA	Yes	For stage 4 metastatic cancer. Redirection does not refer to review of medical necessity or clinical appropriateness.
IA	Yes	For standard of care stage 4 cancer drug use, supported by peer-reviewed, evidence-based literature, and approved by FDA.
IN	Yes	For advanced, metastatic cancer and associated conditions
LA	Yes≠	For stage 4 advanced, metastatic cancer or associated conditions. ≠Exception if clinically equivalent therapy, contains identical active ingredient(s), and proven to have same efficacy.
MS	Yes	For advanced metastatic cancer and associated conditions
NV	Yes	Stage 3 and stage 4 cancer patients for a prescription drug to treat the cancer or any symptom thereof of the covered person
OH	Yes	For stage 4 metastatic cancer and associated conditions
OK	Yes	For advanced metastatic cancer and associated conditions
PA	Yes	For stage 4 advanced, metastatic cancer
TN	Yes^	For cancer and associated conditions ^Exception if step therapy is for AB-rated generic equivalent, interchangeable biological product, or biosimilar product to the equivalent brand drug

State	Step Therapy Prohibited?	Notes
TX	Yes	For stage 4 advanced, metastatic cancer and associated conditions

Appendix F: General Information

- Bone Mineral Density (BMD) T-score was established by the World Health Organization (WHO) as the operational definition for post-menopausal osteoporosis. The T-score is the standard deviation of an individual's BMD from the mean value for young normal women. A normal T-score is considered -1.0 or above.
- The 2020 American Association of Clinical Endocrinologists/American College of Endocrinology Clinical Practice Guidelines use the T-score to diagnosis postmenopausal women with osteoporosis. When an individual's T-score is -2.5 or below, the individual is considered to have osteoporosis or severe osteoporosis in the presence of a fragility fracture (i.e., a fracture sustained from force similar to a fall from a standing position or less that would not have occurred in healthy bone).

V. Dosage and Administration

Drug Name	Indication	Dosing Regimen	Maximum Dose
Denosumab (Prolia, Bildyos, Boncresa, Bosaya, Conexxence, Enoby, Jubbonti, Ospomyv, Osvyrti, Ponlimsi, Stoboclo, denosumab-bnht, denosumab-dssb)	Treatment: PMO, GIO, male osteoporosis	60 mg SC once every 6 months	60 mg/dose
	Oncology: fracture prevention - Men at high risk for fracture receiving ADT for nonmetastatic prostate cancer - Women at high risk for fracture receiving adjuvant aromatase inhibitor therapy for breast cancer		
Denosumab (Xgeva, Aukelso, Bilprevda, Bomyntra, Degevma, Jubereq, Osenvelt, Oziltus, Wyost, Xbryk,	MM Solid tumor - bone metastasis	120 mg SC once every 4 weeks	20 mg/dose
	Giant cell tumor of bone Hypercalcemia of malignancy	120 mg SC every 4 weeks plus 120 mg on Days 8 and 15 of first month of therapy	120 mg/dose

Drug Name	Indication	Dosing Regimen	Maximum Dose
Xtrenbo, denosumab-bnht)			

VI. Product Availability

Drug Name	Availability
Denosumab (Prolia, Bildyos, Boncresa, Bosaya, Conexxence, Enoby, Jubbonti, Ospomyv, Osvyrti, Ponlimsi, Stoboclo, denosumab-bnht, denosumab-dssb)	• Injection (single-use prefilled syringe): 60 mg/mL • *Bildyos only* – Injection (single-use vial): 60 mg/mL
Denosumab (Xgeva, Aukelso, Bilprevda, Bomyntra, Degevma, Jubereq, Osenvelt, Oziltus, Wyost, Xbryk, Xtrenbo, denosumab-bnht)	• Injection (single-use vial): 120 mg/1.7 mL (70 mg/mL) • *Bomyntra and denosumab-bnht only* – Injection (single-dose prefilled syringe): 120 mg/1.7 mL (70 mg/mL)

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Coding Implications
Codes referenced in this clinical policy are for informational purposes only. Inclusion or exclusion of any codes does not guarantee coverage. Providers should reference the most up-to-date sources of professional coding guidance prior to the submission of claims for reimbursement of covered services.

HCPCS Codes	Description
J0897	Injection, denosumab, 1 mg
Q5136	Injection, denosumab-bbdz (jubbonti/wyost), biosimilar, 1 mg
Q5157	Injection, denosumab-bmwo (stoboclo/osenvelt), biosimilar, 1 mg
Q5158	Injection, denosumab-bnht (bomyntra/conexxence), biosimilar, 1 mg
Q5159	Injection, denosumab-dssb (ospomyv/xbryk), biosimilar, 1 mg
Q5161	Injection, denosumab-kyqq (aukelso/bosaya), biosimilar, 1 mg
Q5162	Injection, denosumab-nxxp (bildyos/bilprevda), biosimilar, 1 mg
Q5165	Injection, denosumab-mobz (oziltus), biosimilar, 1 mg
Q5166	Injection, denosumab-desu (osvyrti/jubereq), biosimilar, 1 mg
Q5167	Injection, denosumab-qbde (enoby/xtrenbo), biosimilar, 1 mg
Q5171	Injection, denosumab-mobz (boncresa), biosimilar, 1 mg
Q5173	Injection, denosumab-adet (ponlimsi), biosimilar, 1 mg

Reviews, Revisions, and Approvals	Date	P&T Approval Date
1Q 2022 annual review: updated definition of very high risk for fracture based on 2020 AACE/ACE PMO guidelines; references reviewed and updated.	10.02.21	02.22
For osteoporosis added option (in addition to contraindications or adverse effects) to bypass bisphosphonate trial if member has experienced a loss of BMD, lack of BMD increase, or has had an osteoporotic fracture or fragility fracture while receiving bisphosphonate therapy.	02.07.22	05.22
Template changes applied to other diagnoses/indications and continued therapy section.	10.12.22	
1Q 2023 annual review: no significant changes, reference reviewed and updated.	10.28.22	02.23
Updated Appendix E to include Oklahoma.	06.07.23	
1Q 2024 annual review: no significant changes; for osteoporosis initial criteria, clarified "failure" of generic alendronate is preferred; references reviewed and updated.	10.23.23	02.24
RT4: added new biosimilars Jubbonti and Wyost to policy; added Appendix F to provide clarity on the interpretation of bone mineral density T-scores.	03.14.24	
Updated Appendix E to include Mississippi.	06.05.24	
Added HCPCS code [Q5136].	08.07.24	

Reviews, Revisions, and Approvals	Date	P&T Approval Date
1Q 2025 annual review: per updated prescribing information for Prolia and Jubbonti added boxed warnings for severe hypocalcemia in patients with advanced kidney disease; for prostate and breast cancer added requirement that member does not have bone metastasis; for giant cell tumor of bone localized disease removed option for combination use with interferon alfa per NCCN; references reviewed and updated.	10.22.24	02.25
RT4: added new biosimilars denosumab-dssb, Osenvelt, Ospomyv, Stoboclo, and Xbryk to criteria.	03.06.25	
RT4: added new biosimilars denosumab-bnht, Bomyntra, and Conexxence to criteria.	04.14.25	
Per August SDC: for multiple myeloma or solid tumor, giant cell tumor of bone, hypercalcemia of malignancy, systemic mastocytosis, added redirection to Osenvelt and Wyost if request is for a product other than Osenvelt and Wyost for initial and continuation of therapy requests. RT4: added new biosimilars Bildyos and Bilprevda to criteria. Added new HCPCS codes Q5157, Q5158, Q5159. Added step therapy bypass for IL HIM per IL HB 5395. RT4: added new biosimilars Bosaya, Aukelso, Enoby, and Xtrenbo to criteria	10.01.25	11.25
1Q 2026 annual review: per competitor analysis for MM, removed requirement that member is receiving or initiating therapy (e.g., chemotherapy, transplant) for symptomatic disease; for giant cell tumor of the bone, added additional approval pathway for resectable disease where surgical resection is likely to result in severe morbidity; for initial approval revised approval duration for Medicaid/HIM from 6 to 12 months for all oncology related indications; RT4: added new biosimilars Osvyrti and Jubereq to criteria; references reviewed and updated. Per December SDC, added Bilprevda as an additional preferred biosimilar. RT4: added new biosimilars Boncresa and Oziltus to criteria.	01.15.26	02.26
HCPCS codes added [Q5161, Q5162].	02.19.26	
RT4: added new biosimilar Ponlimsi to criteria. Added state IN to Appendix E.	04.09.26	
Added HCPCS codes Q5165, Q5166, Q5167, and Q5171.	06.02.26	
Per June SDC, removed Commercial and HIM line of business (separated to new policy CP.PCH.63); for osteoporosis and prostate cancer/breast cancer fracture prevention, added Bildyos and Enoby as preferred biosimilars; for all other indications, removed Osenvelt and Wyost as preferred biosimilars and added Xtrenbo as an additional preferred biosimilar.	06.09.26	08.26

Reviews, Revisions, and Approvals	Date	P&T Approval Date
RT4: added new biosimilar Degevma to criteria; added Q5173 HCPCS code; updated Appendix E with revised language for Tennessee.	10.14.26	

Important Reminder

This clinical policy has been developed by appropriately experienced and licensed health care professionals based on a review and consideration of currently available generally accepted standards of medical practice; peer-reviewed medical literature; government agency/program approval status; evidence-based guidelines and positions of leading national health professional organizations; views of physicians practicing in relevant clinical areas affected by this clinical policy; and other available clinical information. The Health Plan makes no representations and accepts no liability with respect to the content of any external information used or relied upon in developing this clinical policy. This clinical policy is consistent with standards of medical practice current at the time that this clinical policy was approved. "Health Plan" means a health plan that has adopted this clinical policy and that is operated or administered, in whole or in part, by Centene Management Company, LLC, or any of such health plan's affiliates, as applicable.

The purpose of this clinical policy is to provide a guide to medical necessity, which is a component of the guidelines used to assist in making coverage decisions and administering benefits. It does not constitute a contract or guarantee regarding payment or results. Coverage decisions and the administration of benefits are subject to all terms, conditions, exclusions, and limitations of the coverage documents (e.g., evidence of coverage, certificate of coverage, policy, contract of insurance, etc.), as well as to state and federal requirements and applicable Health Plan-level administrative policies and procedures.

This clinical policy is effective as of the date determined by the Health Plan. The date of posting may not be the effective date of this clinical policy. This clinical policy may be subject to applicable legal and regulatory requirements relating to provider notification. If there is a discrepancy between the effective date of this clinical policy and any applicable legal or regulatory requirement, the requirements of law and regulation shall govern. The Health Plan retains the right to change, amend or withdraw this clinical policy, and additional clinical policies may be developed and adopted as needed, at any time.

This clinical policy does not constitute medical advice, medical treatment, or medical care. It is not intended to dictate to providers how to practice medicine. Providers are expected to exercise professional medical judgment in providing the most appropriate care, and are solely responsible for the medical advice and treatment of members. This clinical policy is not intended to recommend treatment for members. Members should consult with their treating physician in connection with diagnosis and treatment decisions.

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Note:
For Medicaid members, when state Medicaid coverage provisions conflict with the coverage provisions in this clinical policy, state Medicaid coverage provisions take precedence. Please refer to the state Medicaid manual for any coverage provisions pertaining to this clinical policy.

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