Denosumab - Osteoporosis Medical Drug Criteria Program Summary

POLICY REVIEW CYCLE

Effective Date **Date of Origin**
06-30-2025

FDA LABELED INDICATIONS AND DOSAGE

Agent(s)	FDA Indication(s)	Notes	Ref#
Jubbonti® (denosumab-bbdz) Subcutaneous injection	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		12
Prolia® (denosumab) Subcutaneous injection	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		1
Stoboclo® (denosumab-bmwo) Subcutaneous injection	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		13

Agent(s)	FDA Indication(s)	Notes	Ref#
	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		

See package insert for FDA prescribing information: https://dailymed.nlm.nih.gov/dailymed/index.cfm

CLINICAL RATIONALE

Postmenopausal Osteoporosis	The American Association of Clinical Endocrinologists/American College of Endocrinology joint guidelines for postmenopausal osteoporosis state that there are several pathways to diagnose osteoporosis:(4) • T-score -2.5 or below in the lumbar spine, femoral neck, total proximal femur or distal 1/3 of the radius • Low-trauma spine or hip fracture (regardless of bone mineral density) • T-score between -1.0 and -2.5 and a fragility fracture of proximal humerus, pelvis, or distal forearm • T-score between -1.0 and -2.5 and high FRAX (Fracture Risk Assessment Tool) (or if available, TBS [trabecular bone score]-adjusted FRAX) fracture based on country-specific thresholds The World Health Organization (WHO) has defined T-score criteria as follows:(4) • Normal: T-score -1.0 or above • Osteopenia: T-score between -1.0 and -2.5 • Osteoporosis: T-score at or below -2.5 • Severe or established osteoporosis: -2.5 or below with fragility fracture
Very High Risk Postmenopausal women	The 2020 American Association of Clinical Endocrinology (AACE) Guidelines created a 'very high-risk' category for post-menopausal women with osteoporosis. The following patients are considered to be at very high fracture risk:(4) • Patients with a recent fracture (within the past 12 months) • Patients with fractures while on approved osteoporosis therapy • Patients with multiple fractures • Patients with fractures while on drugs causing skeletal harm (e.g., long-term glucocorticoids) • Patients with a very low T-score (less than -3.0) • Patients with a high-risk for falls or history of injurious falls • Patients with very high fracture probability by FRAX (e.g., major osteoporosis fracture greater than 30%, hip fracture greater than 4.5%) or other validated fracture risk algorithm Patients who have been diagnosed with osteoporosis but do not meet the above definition of very high fracture risk are considered to be at high risk.(4) The AACE recommends alendronate, denosumab, risedronate, and zoledronate as appropriate initial therapy for most osteoporotic patients with high fracture risk. Abaloparatide, denosumab, romosozumab, teriparatide, and zoledronate should be considered for patients unable to use oral therapy and as initial therapy for patients at very high fracture risk.(4)
Men over the age of 50	The Endocrine Society recommends pharmacological treatment for men aged 50 or older at high risk of fracture including, but not limited to:(7)

	• Men who have had a hip or vertebral fracture without major trauma • Men who have not experienced a spine or hip fracture, but whose Bone Mineral Density (BMD) of the spine, femoral neck, and/or total hip is 2.5 standard deviations below the mean of normal young white males • In the US, men who have a T-score between -1.0 and -2.5 in the spine, femoral neck, or total hip plus a 10-year risk of hip fracture greater than or equal to 3% using FRAX. For men outside the US, region-specific guidelines should be considered • Men who are receiving long-term glucocorticoid therapy in pharmacological doses Men at high risk of fracture can be treated with medication approved by regulatory agencies such as the US FDA or the European Medicines Agency (EMA). At the time of this writing of the 2012 Endocrine Society clinical practice guideline for Osteoporosis in Men, alendronate, risedronate, zoledronic acid, and teriparatide were recommended. Denosumab can also be used for men receiving androgen deprivation therapy (ADT) for prostate cancer. The selection of therapeutic agent should be individualized based on factors including fracture history, severity of osteoporosis (T-scores), the risk for hip fracture, patterns of BMD, comorbid conditions, cost, and other factors.(7) The American College of Physicians (ACP) recommends bisphosphonates to reduce the risk for vertebral fracture in men who have clinically recognized osteoporosis.(11)
Treatment	According to the The Bone Health and Osteoporosis Foundation, postmenopausal women and men age 50 and older presenting with the following should be considered for treatment:(3) • A hip or vertebral fracture • A fracture of the pelvis, proximal humerus, or distal forearm in a person with low bone mass or osteopenia • T-score of -2.5 or lower at the femoral neck, total hip, lumbar spine, or 33% radius by DXA • T-score between -1 and -2.5 at the femoral neck or total hip and a 10-year probability of a hip fracture greater than or equal to 3% or a 10-year probability of a major osteoporosis-related fracture greater than or equal to 20% based on the US-adapted FRAX algorithm The Endocrine Society also agrees with these treatment thresholds for men with increased fracture risk.(10) In their 2020 Postmenopausal Osteoporosis Guidelines, the AACE stated that osteoporosis can be diagnosed if there is a fragility fracture in the absence of other metabolic bone disease, independent of the T-score. Thus, patients with a T-score indicating osteopenia, but who have had a fragility fracture of the spine, hip, proximal humerus, pelvis, or distal forearm should be diagnosed with osteoporosis and considered for pharmacologic therapy.(4)

Glucocorticoid-Induced Osteoporosis	The 2022 ACR guideline recommends that all adults starting or continuing therapy with glucocorticoids for greater than 3 months should be assessed for fracture risk. Patients who are at moderate, high, or very high risk of fractures should receive osteoporosis therapy. The guideline categorizes the following risk levels:(8)
	
	• For adults who are 40 years of age or older:
	  ○ Very high risk
	  ▪ Prior osteoporotic fractures OR
	  ▪ T-score less than or equal to -3.5 OR
	  ▪ FRAX 10-year risk of major osteoporotic fracture greater than or equal to 30%, or hip fracture greater than or equal to 4.5% OR
	  ▪ Glucocorticoid use equivalent to greater than or equal to 30 mg/day of prednisone for greater than 30 days OR
	  ▪ Cumulative glucocorticoid doses equivalent to greater than or equal to 5 g/year of prednisone
	  ○ High risk

	▪ T-score less than or equal to -2.5 but greater than -3.5 OR ▪ FRAX 10-year risk of major osteoporotic fracture greater than or equal to 20% and less than 30%, or hip fracture greater than or equal to 3% and less than 4.5% ○ Moderate risk ▪ T-score between -1.0 and -2.4 OR ▪ FRAX 10-year risk of major osteoporotic fracture greater than or equal to 10% and less than 20%, or hip fracture greater than 1% and less than 3% OR ○ Low risk ▪ T-score greater than -1.0 OR ▪ FRAX 10-year risk of major osteoporotic fracture less than 10%, or hip fracture less than 1% • For adults less than 40 years of age: ○ Very high risk ▪ Prior fractures OR ▪ Glucocorticoid use equivalent to greater than or equal to 30 mg/day of prednisone OR ▪ Cumulative glucocorticoid doses equivalent to greater than or equal to 5 g/year of prednisone ○ Moderate risk ▪ Glucocorticoid treatment equivalent to greater than or equal to 7.5 mg/day of prednisone for greater than or equal to 6 months AND z-score less than -3 OR ▪ Significant bone mineral density loss (more than the least significant change of DXA) ○ Low risk ▪ None of the above risk factors other than glucocorticoid treatment Parathyroid hormones/parathyroid hormone related proteins are conditionally recommended over anti-resorptive therapies (bisphosphonate, denosumab) in patients at very high risk of fracture. Denosumab is conditionally recommended over bisphosphonates in individuals at very high risk. Denosumab and parathyroid hormones/parathyroid hormone related proteins are conditionally recommended over oral and IV bisphosphonates in high risk patients. There is no preferred ordered of therapies between bisphosphonates, denosumab, or parathyroid hormones/parathyroid hormone related proteins in patients with moderate risk.(8) Until the effect of concomitant use of osteoporosis agents is better understood, the AACE does not recommend concomitant use of agents for osteoporosis.(4)
Breast Cancer	The National Comprehensive Cancer Network (NCCN) Guidelines in Oncology-Breast Cancer state that:(9) • In postmenopausal patients receiving adjuvant aromatase inhibitor therapy, bisphosphonate or denosumab is acceptable to maintain or improve bone mineral density and reduce risk of fractures. • Patients who are candidates for bisphosphonate therapy for metastatic breast cancer to the bone may also be considered for treatment with denosumab.
Prostate Cancer	The NCCN Guidelines in Oncology-Prostate Cancer state that:(10) • All patients taking androgen deprivation therapy (ADT) should be screened for treatment related bone loss and should be considered as having "secondary osteoporosis" using the FRAX algorithm. Treatment should be based on guidance from the Bone Health and Osteoporosis Foundation. Recommended treatment options include denosumab, zoledronic acid, or alendronate.

Safety	Prolia, Jubbonti, and Stoboclo have the following boxed warnings: Severe hypocalcemia in patients with advanced kidney disease(1,12,13) • Patients with advanced chronic kidney disease (eGFR less than 30 mL/min/1.73^2), are at greater risk of severe hypocalcemia following denosumab 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 or Jubbonti in patients with advanced chronic kidney disease, evaluate for the presence of CKD-MBD. Treatment with denosumab in these patients should be supervised by a healthcare provider with expertise in the diagnosis and management of CKD-MBD. Prolia, Jubbonti, and Stoboclo have the following contraindications:(1,12,13) • Hypocalcemia • Pregnancy • Known hypersensitivity to denosumab products Hypocalcemia must be corrected before initiating Prolia, Jubbonti, or Stoboclo therapy. Adequately supplement all patients with calcium and vitamin D. Prolia, Jubbonti, and Stoboclo are not approved for use in pediatric patients. Hypercalcemia has been reported in pediatric patients with osteogenesis imperfecta treated with denosumab products.(1,12,13)

REFERENCES

Number	Reference
1	Prolia prescribing information. Amgen Pharmaceuticals. March 2024.
2	Reference no longer used.
3	LeBoff MS, Greenspan SL, Inosgna KL et. al. The Clinician's Guide to Prevention and Treatment of Osteoporosis. Osteoporosis Int 33:2049-2102, 2022. https://link.springer.com/content/pdf/10.1007/s00198-021-05900-y.pdf
4	Camacho PM, Petak SM, Binkley N, et al. American Association of Clinical Endocrinologists and American College of Endocrinology clinical practice guidelines for the diagnosis and treatment of postmenopausal osteoporosis – 2020 update. https://www.sciencedirect.com/science/article/pii/S1530891X20428277
5	Reference no longer used.
6	Reference no longer used.
7	Endocrine Society Guideline: Osteoporosis in Men: An Endocrine Society Clinical Practice Guideline 2012. https://academic.oup.com/jcem/article/97/6/1802/2536476
8	Humphrey MB, Russell L, Danila MI, et al. 2022 American College of Rheumatology Guideline for the Prevention and Treatment of Glucocorticoid-Induced Osteoporosis. *Arthritis & Rheumatology*. 2023;75(12):2088-2102. doi:10.1002/art.42646
9	National Comprehensive Cancer Network (NCCN) Clinical Practice Guidelines in Oncology-Breast Cancer, version 3.2024.
10	National Comprehensive Cancer Network (NCCN) Clinical Practice Guidelines in Oncology-Prostate Cancer, version 4.2024.
11	Qaseem A, Forciea MA, McLean RM, et. al. Treatment of Low Bone Density or Osteoporosis to Prevent Fractures in Men and Women: A Clinical Practice Guideline Update from the American College of Physicians. Ann Intern Med. 2017;166:818-839. https://annals.org/aim/fullarticle/2625385/treatment-low-bone-density-osteoporosis-prevent-fractures-men-women-clinical
12	Jubbonti prescribing information. Sandoz Inc. October 2024.
13	Stoboclo prescribing information. Celltrion, Inc. February 2025.

POLICY AGENT SUMMARY – MEDICAL PRIOR AUTHORIZATION

HCPC Codes	Target Brand Agent Name(s)	Target Generic Agent Name(s)	Strength	Targeted MSC	Available MSC	Final Age Limit	Preferred Status
	Jubbonti	denosumab-bbdz inj soln prefilled syringe	60 MG/ML	M ; N ; O ; Y	N		
J0897	Prolia	denosumab inj soln prefilled syringe	60 MG/ML	M ; N ; O ; Y	N		
	Stoboclo	denosumab-bmwo inj soln prefilled syringe	60 MG/ML	M ; N ; O ; Y	N		

POLICY AGENT SUMMARY QUANTITY LIMIT

Target Brand Agent Name(s)	Target Generic Agent Name(s)	Strength	QL Amount	Dose Form	Day Supply	Duration	Addtl QL Info	Allowed Exceptions	Targeted NDCs When Exclusions Exist
Jubbonti	denosumab-bbdz inj soln prefilled syringe	60 MG/ML	1	Injection	180	DAYS			
Prolia	denosumab inj soln prefilled syringe	60 MG/ML	1	Injection	180	DAYS			
Stoboclo	denosumab-bmwo inj soln prefilled syringe	60 MG/ML	1	Syringe	180	DAYS			

CLIENT SUMMARY – PRIOR AUTHORIZATION

Target Brand Agent Name(s)	Target Generic Agent Name(s)	Strength	Client Formulary
Jubbonti	denosumab-bbdz inj soln prefilled syringe	60 MG/ML	Commercial ; HIM ; ResultsRx
Prolia	denosumab inj soln prefilled syringe	60 MG/ML	Commercial ; HIM ; ResultsRx
Stoboclo	denosumab-bmwo inj soln prefilled syringe	60 MG/ML	Commercial ; HIM ; ResultsRx

CLIENT SUMMARY – QUANTITY LIMITS

Target Brand Agent Name(s)	Target Generic Agent Name(s)	Strength	Client Formulary
Jubbonti	denosumab-bbdz inj soln prefilled syringe	60 MG/ML	Commercial ; HIM ; ResultsRx
Prolia	denosumab inj soln prefilled syringe	60 MG/ML	Commercial ; HIM ; ResultsRx
Stoboclo	denosumab-bmwo inj soln prefilled syringe	60 MG/ML	Commercial ; HIM ; ResultsRx

PRIOR AUTHORIZATION CLINICAL CRITERIA FOR APPROVAL

Module	Clinical Criteria for Approval
	Initial Evaluation

Module	Clinical Criteria for Approval
	Target Agent(s) will be approved when ALL of the following are met: 1. ONE of the following: A. The patient has a diagnosis of osteoporosis and ALL of the following: 1. ONE of the following: A. The patient's sex is male and ONE of the following: 1. The patient's age is 50 years or over **OR** 2. The requested agent is medically appropriate for the patient's age and sex **OR** B. The patient's sex is female and ONE of the following: 1. The patient is postmenopausal **OR** 2. The requested agent is medically appropriate for the patient's sex and menopause status **AND** 2. The patient's diagnosis was confirmed by ONE of the following: A. A fragility fracture in the hip or spine **OR** B. A T-score of -2.5 or lower **OR** C. A T-score of -1.0 to -2.5 and ONE of the following: 1. A fragility fracture of the proximal humerus, pelvis, or distal forearm **OR** 2. A FRAX 10-year probability for major osteoporotic fracture of greater than or equal to 20% **OR** 3. A FRAX 10-year probability of hip fracture of greater than or equal to 3% **AND** 3. ONE of the following: A. The patient is at a very high fracture risk as defined by ONE of the following: 1. Patient had a recent fracture (within the past 12 months) **OR** 2. Patient had fractures while on approved osteoporosis therapy **OR** 3. Patient has had multiple fractures **OR** 4. Patient had fractures while on drugs causing skeletal harm (e.g., long-term glucocorticoids) **OR** 5. Patient has a very low T-score (less than -3.0) **OR** 6. Patient is at high risk for falls or has a history of injurious falls **OR** 7. Patient has a very high fracture probability by FRAX (e.g., major osteoporosis fracture greater than 30%, hip fracture greater than 4.5%) or by other validated fracture risk algorithm **OR** B. The patient has tried and had an inadequate response to a bisphosphonate (medical records required) **OR** C. The patient has an intolerance or hypersensitivity to a bisphosphonate (medical records required) **OR** D. The patient has an FDA labeled contraindication to ALL bisphosphonates (medical records required) **OR** B. The patient is requesting the agent for osteopenia (osteoporosis prophylaxis) and ALL of the following: 1. ONE of the following: A. The patient's sex is male and ONE of the following: 1. The patient's age is 50 years or over **OR** 2. The requested agent is medically appropriate for the patient's age and sex **OR** B. The patient's sex is female and ONE of the following: 1. The patient is postmenopausal **OR** 2. The requested agent is medically appropriate for the patient's sex and menopause status **AND** 2. BOTH of the following: A. The patient has osteopenia, defined as a T-score between -1.0 to -2.5 **AND** B. ONE of the following:

Module	Clinical Criteria for Approval
	1. A fragility fracture of the proximal humerus, pelvis, or distal forearm **OR** 2. A 10-year probability of a hip fracture greater than or equal to 3% per FRAX **OR** 3. A 10-year probability of a major osteoporosis-related fracture greater than or equal to 20% per FRAX **AND** 3. ONE of the following: A. The patient has tried and had an inadequate response to a bisphosphonate (medical records required) **OR** B. The patient has an intolerance or hypersensitivity to a bisphosphonate (medical records required) **OR** C. The patient has an FDA labeled contraindication to ALL bisphosphonates (medical records required) **OR** C. The patient has a diagnosis of breast cancer and BOTH of the following: 1. The patient is currently receiving aromatase inhibitor therapy **AND** 2. ONE of the following: A. The patient has tried and had an inadequate response to a bisphosphonate (medical records required) **OR** B. The patient has an intolerance or hypersensitivity to a bisphosphonate (medical records required) **OR** C. The patient has an FDA labeled contraindication to ALL bisphosphonates (medical records required) **OR** D. The patient has a diagnosis of nonmetastatic prostate cancer and BOTH of the following: 1. The patient is currently receiving androgen deprivation therapy (ADT) **AND** 2. ONE of the following: A. The patient has tried and had an inadequate response to a bisphosphonate (medical records required) **OR** B. The patient has an intolerance or hypersensitivity to a bisphosphonate (medical records required) **OR** C. The patient has an FDA labeled contraindication to ALL bisphosphonates (medical records required) **OR** E. The patient has a diagnosis of glucocorticoid-induced osteoporosis and ALL of the following: 1. The patient is either initiating or currently taking glucocorticoids in a daily dosage equivalent to 7.5 mg or higher of prednisone **AND** 2. The patient's expected current course of therapy of glucocorticoids is for a period of at least 6 months **AND** 3. ONE of the following: A. The patient is less than 40 years of age AND has ONE of the following: 1. A prior fracture **OR** 2. Either initiating or currently taking glucocorticoids that is equivalent to a prednisone dose that is greater than or equal to 30 mg/day **OR** 3. Either initiating or currently taking glucocorticoids that is equivalent to a cumulative prednisone dose of greater than or equal to 5 g/year **OR** B. The patient is 40 years of age or greater AND has one of the following: 1. A prior osteoporotic fracture **OR** 2. A T-score of less than or equal to -2.5 **OR** 3. A FRAX 10-year probability for major osteoporotic fracture of greater than or equal to 20% **OR** 4. A FRAX 10-year risk probability for hip fracture of greater than or equal to 3% **OR** 5. Either initiating or currently taking glucocorticoids that is equivalent to a prednisone dose that is greater than or equal to 30 mg/day for greater than 30 days **OR**

Module	Clinical Criteria for Approval
	6. Either initiating or currently taking glucocorticoids that is equivalent to a cumulative prednisone dose of greater than or equal to 5 g/year **OR** C. The patient has tried and had an inadequate response to a bisphosphonate (medical records required) **OR** D. The patient has an intolerance or hypersensitivity to a bisphosphonate (medical records required) **OR** E. The patient has an FDA labeled contraindication to ALL bisphosphonates (medical records required) **AND** 2. The patient will NOT be using the requested agent in combination with a bisphosphonate, another form of denosumab (e.g., Xgeva), romosozumab-aqqg, or a parathyroid hormone analog for osteoporosis (e.g., abaloparatide, teriparatide) **AND** 3. If patient has a diagnosis of advanced chronic kidney disease (eGFR less than 30 mL/min/1.73^2 including dialysis-dependent patients), then BOTH of the following: A. Prior to initiating therapy with the requested agent, the patient will be evaluated for the presence of chronic kidney disease-mineral bone disorder (CKD-MBD) **AND** B. If the patient has CKD-MBD, the prescriber is a specialist in the area of the patient's diagnosis (e.g., nephrologist) or the prescriber has consulted with a specialist in the area of the patient's diagnosis **AND** 4. The patient does NOT have any FDA labeled contraindications to the requested agent **AND** 5. ONE of the following: A. The requested quantity (dose) does NOT exceed the program quantity limit **OR** B. Both of the following: 1. The requested quantity (dose) exceeds the program quantity limit **AND** 2. The requested quantity (dose) is within FDA labeled dosing for the requested indication **Length of approval:** 12 months **Renewal Evaluation** **Target Agent(s)** will be approved when ALL of the following are met: 1. The patient has been previously approved for the requested agent through the plan's Prior Authorization process [Note: patients not previously approved for the requested agent will require initial evaluation review] **AND** 2. The patient has had clinical benefit with the requested agent **AND** 3. The patient will NOT be using the requested agent in combination with a bisphosphonate, another form of denosumab (e.g., Xgeva), romosozumab-aqqg, or a parathyroid hormone analog for osteoporosis (e.g., abaloparatide, teriparatide) **AND** 4. The patient does NOT have any FDA labeled contraindications to the requested agent **AND** 5. ONE of the following: A. The requested quantity (dose) does NOT exceed the program quantity limit **OR** B. Both of the following: 1. The requested quantity (dose) exceeds the program quantity limit **AND** 2. The requested quantity (dose) is within FDA labeled dosing for the requested indication **Length of Approval:** 12 months

