

Corporate Medical Policy

Denosumab (Prolia™, XGEVA™)

File Name:	denosumab
Origination:	3/2011
Last CAP Review:	9/2011
Next CAP Review:	9/2012
Last Review:	9/2011

Description of Procedure or Service

Receptor activator of nuclear factor- κ B ligand (RANKL), a protein expressed by osteoblastic stromal cells, binds to receptor activator of nuclear factor- κ B (RANK) and is the primary mediator of osteoclast differentiation, activation, and survival. RANKL is responsible for osteoclast-mediated bone resorption in a broad range of conditions. Osteoprotegerin, a soluble RANKL decoy receptor that binds RANKL, is the key endogenous regulator of the RANKL–RANK pathway.

Denosumab (formerly known as AMG 162, Amgen) is a fully human monoclonal antibody (IgG2) that binds to RANKL with high affinity and specificity and blocks the interaction of RANKL with RANK, mimicking the endogenous effects of osteoprotegerin. In a phase 1 dose-escalation study, a single subcutaneous injection of denosumab resulted in a dose-dependent decrease in bone resorption, as measured by changes in serum and urinary N-telopeptide, markers of osteoclastic bone resorption.

Denosumab is marketed under the trade name XGEVA™ for the prevention of skeletal-related events in cancer patients with bone metastases from solid tumors. The same drug is marketed under the trade name Prolia™ for postmenopausal osteoporosis and as treatment to increase bone mass in patients with prostate and breast cancer who are on hormone ablation therapy.

*****Note: This Medical Policy is complex and technical. For questions concerning the technical language and/or specific clinical indications for its use, please consult your physician.**

Policy

BCBSA will provide coverage for denosumab when it is determined to be medically necessary because the medical criteria and guidelines shown below are met.

Benefits Application

This medical policy relates only to the services or supplies described herein. Please refer to the Member's Benefit Booklet for availability of benefits. Member's benefits may vary according to benefit design; therefore member benefit language should be reviewed before applying the terms of this medical policy.

When denosumab is covered

Prolia™ may be considered medically necessary for members who have failed or are unable to tolerate at least one oral bisphosphonate, or for whom oral bisphosphonate therapy is contraindicated, (including inability to swallow or to remain in an upright position after oral bisphosphonate administration), for these conditions:

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- Treatment of postmenopausal women with osteoporosis at high risk for fracture (those who have had an osteoporotic fracture, or have multiple risk factors for fracture); OR
- Prevention of osteoporosis in persons receiving aromatase inhibitors (anastrozole, letrozole, exemestane)

Prolia™ may also be considered medically necessary for:

- Treatment to increase bone mass in women at high risk for fracture receiving adjuvant aromatase inhibitor therapy for breast cancer; OR
- Treatment to increase bone mass in men at high risk for fracture receiving androgen deprivation therapy for nonmetastatic prostate cancer.

XGEVA™ may be considered medically necessary for:

- Prevention of skeletal-related events in patients with bone metastases from solid tumors.

When denosumab is not covered

Denosumab (Prolia™ and XGEVA™) is considered investigational for the following indications (not an all inclusive list):

- Giant-cell tumor of bone
- Multiple myeloma
- Osteogenesis imperfect
- Primary bone sarcomas (Ewing's sarcoma and osteosarcoma)
- Rheumatoid arthritis

Policy Guidelines

The same active ingredient (denosumab) is found in Prolia™ and XGEVA™. Patient should not receive both drugs.

Denosumab is contraindicated in patients with hypocalcemia. Hypocalcemia should be corrected prior to initiating denosumab therapy. Patients with creatinine clearance less than 30mL/min or receiving dialysis are at risk for hypocalcemia.

Denosumab is not recommended for use in pediatric patients.

There are no adequate and well-controlled studies of Prolia™ in pregnant women and nursing mothers. Prolia™ should be used during pregnancy and lactation only if the importance of the drug to the mother justified the potential risk to the fetus/infant.

Billing/Coding/Physician Documentation Information

This policy may apply to the following codes. Inclusion of a code in this section does not guarantee that it will be reimbursed. For further information on reimbursement guidelines, please see Administrative Policies on the Blue Cross Blue Shield of North Carolina web site at www.bcbsnc.com. They are listed in the Category Search on the Medical Policy search page.

Applicable codes: J0897, J3490, J3590

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BCBSNC may request medical records for determination of medical necessity. When medical records are requested, letters of support and/or explanation are often useful, but are not sufficient documentation unless all specific information needed to make a medical necessity determination is included.

Scientific Background and Reference Sources

McClung MR, Lewiecki EM, Cohen SB, et al. (February 2006). Denosumab in Postmenopausal Women with Low Bone Mineral Density. *N Engl J Med* 2006; 354:821-831

Ellis GK, Bone HG, Chlebowski R, et al. (October 2008). Randomized Trial of Denosumab in Patients Receiving Adjuvant Aromatase Inhibitors for Nonmetastatic Breast Cancer. 26:4875-4882

U.S. Food and Drug Administration (FDA). FDA approves new injectable osteoporosis treatment for postmenopausal women. FDA News. Rockville, MD: FDA; June 1, 2010. Retrieved 3/23/11 from: <http://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm214150.htm>.

Amgen, Inc. Prolia™ (denosumab) injection for subcutaneous use. Prescribing Information. Thousand Oaks, CA:Amgen; 2010. Retrieved 3/23/11 from: http://pi.amgen.com/united_states/prolia/prolia_pi.pdf.

U.S. Food and Drug Administration (FDA). FDA approves Xgeva to help prevent cancer-related bone injury. FDA News. Rockville, MD: FDA; November 19, 2010. Retrieved 3/23/11 from: <http://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm234346.htm>

Amgen, Inc. Xgeva (denosumab). Prescribing Information. Thousand Oaks, CA: Amgen; 2010. Retrieved 3/23/11 from: http://www.amgen.com/medpro/products_xgeva.html.

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.

Amgen, Inc. Prolia™ (denosumab) injection for subcutaneous use. Prescribing Information. Thousand Oaks, CA:Amgen; Revised 9/2011. Retrieved 9/20/11 from: http://pi.amgen.com/united_states/prolia/prolia_pi.pdf

Medical Director review – October 2011

Policy Implementation/Update Information

7/1/2011 New policy developed. BCBSA will provide coverage for denosumab when it is determined to be medically necessary because the medical criteria and guidelines outlined in the policy are met. Prolia™ may be considered medically necessary for treatment of postmenopausal women with osteoporosis at high risk for fracture. XGEVA™ may be considered medically necessary for prevention of skeletal-related events in patients with bone metastases from solid tumors. Notification given 7/1/2011 for effective date 9/29/2011. (adn)

10/1/2011 Added the following to Prolia in the When Denosumab Is Covered section: Prolia™ may be considered medically necessary for members who have failed or are unable to tolerate at least one oral bisphosphonate, or for whom oral bisphosphonate therapy is contraindicated, (including inability to swallow or to remain in an upright position after oral bisphosphonate administration), AND for: Treatment of postmenopausal women with osteoporosis at high risk for fracture (those who have had an osteoporotic fracture, or have multiple risk factors for fracture); OR Prevention of osteoporosis in persons

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receiving aromatase inhibitors (anastrozole, letrozole, exemestane); OR Treatment to increase bone mass in women at high risk for fracture receiving adjuvant aromatase inhibitor therapy for breast cancer; OR Treatment to increase bone mass in men at high risk for fracture receiving androgen deprivation therapy for nonmetastatic prostate cancer. The following statements were deleted from the When Denosumab Is Not Covered section: “Bone loss associated with hormone-ablation therapy in breast cancer or prostate cancer” and “Use of denosumab is not approved for use in pregnant women, nursing mothers or pediatric patients.” The statement: “The same active ingredient (denosumab) is found in Prolia™ and XGEVA™. Patient should not receive both drugs” was added to Policy Guidelines. The statements “Denosumab is not recommended for use in pediatric patients” and “There are no adequate and well-controlled studies of Prolia™ in pregnant women and nursing mothers. Prolia™ should be used during pregnancy and lactation only if the importance of the drug to the mother justified the potential risk to the fetus/infant” were also added to the Policy Guidelines. Codes J3490 and J3590 were added to the Billing/Coding section. (adn)

- 10/11/11 Specialty Matched Consultant Advisory Panel review 9/28/11. Policy accepted as written. (adn)
- 10/25/11 *When Denosumab Is Covered* section revised to clarify requirement for oral biphosphonate. (adn)
- 1/1/12 Code C9272 deleted and replaced with J0897 in the Billing/Coding section. (adn)

Medical policy is not an authorization, certification, explanation of benefits or a contract. Benefits and eligibility are determined before medical guidelines and payment guidelines are applied. Benefits are determined by the group contract and subscriber certificate that is in effect at the time services are rendered. This document is solely provided for informational purposes only and is based on research of current medical literature and review of common medical practices in the treatment and diagnosis of disease. Medical practices and knowledge are constantly changing and BCBSNC reserves the right to review and revise its medical policies periodically.