BlueCross BlueShield of Arizona
An Independent Licensee of the Blue Cross and Blue Shield Association

MEDICAL COVERAGE GUIDELINES
SECTION: DRUGS

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XGEVA™ (denosumab) INJECTION

Coverage for services, procedures, medical devices and drugs are dependent upon benefit eligibility as outlined in the member's specific benefit plan. This Medical Coverage Guideline must be read in its entirety to determine coverage eligibility, if any.

The section identified as "Description" defines or describes a service, procedure, medical device or drug and is in no way intended as a statement of medical necessity and/or coverage.

The section identified as "Criteria" defines criteria to determine whether a service, procedure, medical device or drug is considered medically necessary or experimental or investigational.

State or federal mandates, e.g., FEP program, may dictate that any drug, device or biological product approved by the U.S. Food and Drug Administration (FDA) may not be considered experimental or investigational and thus the drug, device or biological product may be assessed only on the basis of medical necessity.

Medical Coverage Guidelines are subject to change as new information becomes available.

For purposes of this Medical Coverage Guideline, the terms "experimental" and "investigational" are considered to be interchangeable.

Description:

XGEVA™ (denosumab) is a human monoclonal antibody and a RANK Ligand (RANKL) inhibitor indicated for the prevention of skeletal-related events (SKEs) (e.g., pathologic fractures and spinal cord compression) in individuals with bone metastases from solid tumors. When tumor cells invade bone, bone cells increase production of RANKL which drives formation and survival of osteoclasts, leading to bone resorption and destruction. XGEVA binds RANKL, preventing maturation of osteoclasts and decreasing bone resorption and destruction.

XGEVA (denosumab) INJECTION (cont.)

Criteria:

- XGEVA for the prevention of skeletal-related events in individuals with bone metastases from solid tumors is considered ***medically necessary*** with documentation of **ALL** of the following:

  1. Individual is age 18 years of age or older
  2. Not being treated for prevention of skeletal-related events in multiple myeloma
  3. Not concurrently treated with another agent with the same active ingredient denosumab
  4. No hypocalcemia present
  5. No osteonecrosis identified as documented by oral exam
  6. Is currently not pregnant

- XGEVA for the treatment of giant cell tumor of the bone in individuals 13 years of age or older is considered ***medically necessary*** with documentation of **ALL** of the following:

  1. Giant cell tumor of bone is unresectable **OR** surgical resection is likely to result in severe morbidity
  2. Not concurrently treated with another agent with the same active ingredient denosumab
  3. Individual is skeletally mature (radiographic evidence of epiphyseal closure)
  4. No hypocalcemia present
  5. No osteonecrosis identified as documented by oral exam
  6. Is currently not pregnant

- XGEVA for all other indications not previously listed or if above criteria not met is considered ***experimental or investigational*** based upon:

  1. Insufficient scientific evidence to permit conclusions concerning the effect on health outcomes, and
  2. Insufficient evidence to support improvement of the net health outcome.

XGEVA (denosumab) INJECTION (cont.)

Resources:

FDA Product Approval Information for Xgeva:

- FDA-approved indication: For the prevention of skeletal-related events in patients with bone metastases from solid tumors. Important limitation of use: Xgeva is not indicated for the prevention of skeletal-related events in patients with multiple myeloma.

- FDA-approved dosage: The recommended dose of Xgeva is 120 mg administered as a subcutaneous injection every 4 weeks in the upper arm, upper thigh, or abdomen. Correct hypocalcemia prior to initiating Xgeva. Monitor calcium levels and administer calcium, magnesium and vitamin D as necessary to treat or prevent hypocalcemia. Monitor for symptoms of osteonecrosis. Perform an oral examination and appropriate preventive dentistry prior to the initiation of Xgeva and periodically during Xgeva therapy. Advise females of reproductive potential to use highly effective contraception during therapy, and for at least 5 months after the last dose of Xgeva.

  Pediatric patients: Safety and efficacy has not been established.

FDA Product Approval Information for Xgeva: (cont.)

- FDA-approved indication: Treatment of giant cell tumor of bone that is unresectable or where surgical resection is likely to result in severe morbidity.

- FDA-approved dosage: The recommended dose of Xgeva is 120 mg administered as a subcutaneous injection every 4 weeks with additional 120 mg doses on Days 8 and 15 of the first month of therapy in the upper arm, upper thigh, or abdomen. Correct hypocalcemia prior to initiating Xgeva. Monitor calcium levels and administer calcium, magnesium and vitamin D as necessary to treat or prevent hypocalcemia. Monitor for symptoms of osteonecrosis. Perform an oral examination and appropriate preventive dentistry prior to the initiation of Xgeva and periodically during Xgeva therapy. Advise females of reproductive potential of potential risk to the fetus and to use highly effective contraception.

  Pediatric patients: The safety and efficacy of Xgeva have not been established in pediatric patients except in skeletally mature adolescents with giant cell tumors in the bone.