Bisphosphonates (Intravenous [IV]) and Monoclonal Antibodies in the Treatment of Osteoporosis and Their Other Indications.

FIRST COAST SERVICE OPTIONS
MAC - PART A/B
LOCAL COVERAGE DETERMINATION

LCD Database ID Number
L33270

Contractor Name
First Coast Service Options, Inc.

Contractor Number
09101 – Florida
09201 – Puerto Rico/Virgin Islands
09102 – Florida
09202 – Puerto Rico
09302 – Virgin Islands

Contractor Type
MAC – Part A and B

LCD Title
Bisphosphonates (Intravenous [IV]) and Monoclonal Antibodies in the Treatment of Osteoporosis and Their Other Indications

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CMS National Coverage Policy

Language quoted from CMS National Coverage Determination (NCDs) and coverage provisions in interpretive manuals are italicized throughout the Local Coverage Determination (LCD). NCDs and coverage provisions in interpretive manuals are not subject to the LCD Review Process (42 CFR 405.860[b] and 42 CFR 426 [Subpart D]). In addition, an administrative law judge may not review an NCD. See §1869(f)(1)(A)(i) of the Social Security Act.

Unless otherwise specified, italicized text represents quotation from one or more of the following CMS sources:

CMS Manual System, Pub. 100-08, Medicare Program Integrity Manual, Chapter 13, Section 13

CMS Manual System, Pub. 100-02, Medicare Benefit Policy Manual, Chapter 15, Section 50
Indications and Limitations of Coverage and/or Medical Necessity

Indications

This LCD addresses “incident to” drugs that are not self-administered for certain patients with osteoporosis. The other indications for these drugs are also addressed. Osteoporosis is characterized by decreased bone mass and increased fracture risk, most commonly at the spine, hip, and wrist. The diagnosis can be confirmed by a finding of low bone mass, evidence of fracture on x-ray, a history of osteoporotic fracture, or height loss or kyphosis indicative of vertebral fracture. While osteoporosis occurs in both men and women, it is most common among women following menopause. In healthy people, bone formation and resorption are closely linked; old bone is resorbed and replaced by newly formed bone. In postmenopausal osteoporosis, bone resorption exceeds bone formation, leading to bone loss and increased risk of fracture. The World Health Organization (WHO) defines osteoporosis in a postmenopausal woman or a man over the age of 50 as a bone mineral density (BMD) T-score less than or equal to -2.5 at the total hip, femoral neck, or lumbar spine (at least two vertebral levels measured in the posterior-anterior projection, not the lateral projection) as noted below (refer also to LCD for Bone Mineral Density Studies.

- Normal: T-score above (i.e., better than) or equal to -1.0
- Osteopenia: T-score between -1.0 and -2.5
- Osteoporosis: T-score below (i.e., worse than) or equal to -2.5

In addition to diagnosis through densitometry, osteoporosis can be diagnosed clinically, regardless of the T-score. The presence of a fragility fracture constitutes a clinical diagnosis of osteoporosis. It is important to distinguish between risk factors for osteoporosis as defined by BMD and risk factors for osteoporotic fracture. The use of BMD T-scores to assess fracture risk can be markedly improved by combining BMD with information about other risk factors, particularly the woman’s age and fracture history. The major risk factors in postmenopausal women are advanced age, genetics, lifestyle factors (e.g., low calcium and vitamin D intake, smoking, and heavy alcohol consumption), thinness, and menopausal status. Because nearly 50% of postmenopausal women in the community over
the age of 50 years who suffer an osteoporotic fracture do not have osteoporosis as defined by a BMD test, the WHO developed the fracture risk assessment tool (FRAX) to identify clinical risk factors of patients at high risk for osteoporotic fractures:

- Age
- Sex
- Prior fragility fracture after age 50
- History of corticosteroid use (5 mg per day or more for three months or longer)
- Parental history of hip fracture
- Rheumatoid arthritis
- Secondary osteoporosis (e.g., type 1 diabetes, osteogenesis imperfecta in adults, longstanding hyperthyroidism, hypogonadism, premature menopause (before age 40), chronic malabsorption and chronic liver disease)
- Current smoker
- Alcohol use of greater than 2 medium glasses of wine or beer per day
- Body Mass Index (BMI) (less than 21 kg/m2)

Other secondary causes of osteoporosis include the following:

- Oral glucocorticosteroid therapy for longer than 3 months
- Hypogonadism
- Transplant history
- Obesity surgery
- Malabsorption disease
- Aromatase therapy for breast cancer
- Excess urinary calcium excretion
- Vitamin D deficiency
- Hypocalcemia
- Multiple myeloma
- Endocrine disorders such as hyperthyroidism, Cushing’s syndrome, and disorders of collagen structures
- Renal failure (increase bone resorption, or decreased bone formation leading to renal osteodystrophy)
- Paget’s disease
- Liver/biliary disease
- Metastatic cancer involving bone

Medical management focused on lifestyle may be all that is needed for postmenopausal women who are at low risk for osteoporotic fracture. The North American Menopause Society (NAMS) recommends adding osteoporosis drug therapy in the following populations:

- All postmenopausal women who have had an osteoporotic vertebral or hip fracture
- All postmenopausal women who have had BMD values consistent with osteoporosis (i.e., T-scores equal to or worse than -2.5) at the lumbar spine, femoral neck, or total hip region

In order to be covered by Medicare, a drug or biological must be safe and effective and otherwise reasonable and medically necessary. Drugs and biologicals approved for marketing by the Food and Drug Administration (FDA) are considered safe and effective when used for indications specified in the FDA labeling. The FDA labeling lists the safe and effective indications, dosage, and frequency of the agents. The Centers for Medicare and Medicaid Services (CMS) Medicare Benefit Policy Manual, Pub. 100-02, chapter 15, section 50 states the following:

The Medicare program provides limited benefits for outpatient drugs that are furnished “incident to” a physician’s service provided that the drugs are not usually self-administered by the patients who take them. Generally, drugs and biologicals are covered only if all of the following requirements are met:

- They meet the definition of drugs or biologicals;
- They are of the type that are not usually self-administered;
They meet all of the general requirements for coverage of items as incident to a physician’s services;

They are reasonable and necessary for the diagnosis or treatment of the illness or injury for which they are administered according to accepted standards of medical practice;

They are not excluded as noncovered immunizations; and

They have not been determined by the FDA to be less than effective.

In addition to FDA approved indications, Medicare may consider coverage of off-label uses based on guidance provided in the Medicare Benefit Policy Manual, Pub. 100-02, chapter 15, section 50.4.2. This manual section indicates the following:

Unlabeled Use of Drugs:

FDA approved drugs used for indications other than what is indicated on the official label may be covered under Medicare if the contractor determines the use to be medically accepted, taking into consideration the major drug compendia, authoritative medical literature and/or accepted standards of medical practice. These decisions are made by the contractor on a case-by-case basis.

If the drug use is not on the FDA label, and is not included in one of the compendium approved by CMS (American Hospital formulary Services (AHFS), Clinical Pharmacology, NCCN Drugs and Biologicals Compendium and/or Thomson Micromedex DrugDex®) and the Medicare Administrative Contractor Jurisdiction 9 (MAC J9) has not published an LCD or article covering the off-label use, the drug use would not be considered reasonable and necessary, and, therefore not allowed. Not only does the indication for the use of the drug need to meet medical necessity requirements, but the route of administration is also subject to medical necessity criteria.

Contractors must continue to apply the policy that not only is the drug medically reasonable and necessary for any individual claim, but also that the route of administration is medically reasonable and necessary. That is, if a drug is available in both oral and injectable forms, the injectable form of the drug must be medically reasonable and necessary as compared to using the oral form.

Medication given by injection (parenterally) is not covered if standard medical practice indicates that the administration of the medication by mouth (orally) is effective and is an accepted or preferred method of administration.

Medical necessity is not demonstrated in the cases where a patient has not taken the oral form of a medication before the IV form of the drug, either for patient or provider convenience purposes, or for financial or emotional reasons, and these claims will be denied.

**Bisphosphonates**

The following bisphosphonate injections (administered intravenously [IV]) will be considered medically reasonable and necessary when administered as outlined in this LCD. The coverage of IV bisphosphonates must be supported in the medical record. The documentation should include the following information:

- Criteria for the diagnosis of osteoporosis, and
- History of treatment as related to progression of disease and ongoing risk factors, and
- Description of treatment failure, or contraindication, or adverse side effects, of oral or self administered drugs for osteoporosis as applicable to the patient that supports IV therapy in lieu of standard oral treatment protocol.

The following IV bisphosphonate injections are considered medically reasonable and necessary when administered as outlined in this LCD:

- Ibandronate sodium injection (Boniva®)
- Pamidronate (Aredia®)
- Zoledronic acid injection (Reclast®)
- Zoledronic acid injection (Zometa®)

**Boniva®** is a bisphosphonate that inhibits osteoclast activity and reduces bone resorption and turnover, leading to, on average, a net gain in bone mass.

Given the oral equivalent and the availability of Boniva® tablets, and the Medicare manual language on the reasonable and necessary criteria for route of admission, the IV administration is allowed under the following circumstances:
Bisphosphonates (Intravenous [IV]) and Monoclonal Antibodies in the Treatment of Osteoporosis and Their Other Indications

- Patient has a diagnosis of esophageal stricture, achalasia, or other severe esophageal dysmotility disorder; OR
- Patient has a history of severe malabsorption making use of oral bisphosphonates ineffective; OR
- Patient has an inability to stand or sit upright for 60 minutes; OR
- Patient has documented adverse effects following the initiation of treatment of the oral form of the medication that required the withdrawal of the oral form of the medication.

**FDA Indication for Boniva® Injection:**
- Treatment of postmenopausal osteoporosis in women

**Off-label Indications for Boniva® Injection:**
- Corticosteroid-induced osteoporosis
- Paget’s disease
- Bone metastases in patients with prostate cancer

**Aredia®** is a bisphosphonate which is administered intravenously, is used to inhibit bone resorption and to decrease serum calcium.

**FDA Indications for Aredia®**
- Hypercalcemia of Malignancy – Aredia®, in conjunction with adequate hydration, is indicated for the treatment of moderate or severe hypercalcemia associated with malignancy, with or without bone metastases.
- Paget’s Disease – Aredia® is indicated for the treatment of patients with moderate to severe Paget’s disease of bone.
- Osteolytic Bone Metastases of Breast Cancer and Osteolytic Lesions of Multiple Myeloma – Aredia® is indicated, in conjunction with standard antineoplastic therapy, for the treatment of osteolytic bone metastases of breast cancer and osteolytic lesions of multiple myeloma

**Off-label Indications for Aredia®**
- Treatment of postmenopausal osteoporosis
- Treatment of the prevention of glucocorticoid-induced osteoporosis

**Zoledronic acid (Reclast® and Zometa®)** is a bisphosphonic acid, which is an inhibitor of osteoclastic bone resorption. Zoledronic acid binds to the bone matrix, which decreases osteoclastic activity, prevents bone resorption and skeletal calcium release induced by various stimulatory factors released by tumors.

**FDA Indications for Reclast® Injection:**
- Treatment of osteoporosis in postmenopausal women
- Treatment of osteoporosis in men
- Treatment and prevention of glucocorticoid-induced osteoporosis in men and women who are either initiating or continuing systemic glucocorticoids in a daily dosage equivalent to 7.5 mg or greater of prednisone and who are expected to remain on glucocorticoids for at least 12 months
- Treatment for Paget’s disease of the bone with elevations in serum alkaline phosphatase of two times or higher than upper limit of the age-specific normal reference range, or those who are symptomatic, or those at risk for complications from their disease, to induce remission (normalization of serum alkaline phosphatase).

**FDA Indications for Zometa® Injection:**
- Hypercalcemia of malignancy
- Multiple myeloma
- Bone metastases from solid tumors in conjunction with standard antineoplastic therapy, including
  - Bone metastases from multiple myeloma,
Bisphosphonates (Intravenous [IV]) and Monoclonal Antibodies in the Treatment of Osteoporosis and Their Other Indications.

- breast carcinoma,
- prostate carcinoma, and
- other solid tumors

Note: Prostate cancer should have progressed after treatment with at least one hormonal therapy.

**Off-label Indication for Zometa® Injection:**
- Drug-induced osteopenia, secondary to androgen-deprivation therapy in prostate cancer patients (prophylaxis).

**Monoclonal Antibodies - RANK ligand (RANKL) Inhibitors:**
The following monoclonal antibodies injections (administered subcutaneously [SQ]) will be considered medically reasonable and necessary when administered as outlined in this LCD. The coverage of SQ monoclonal antibodies must be supported in the medical record. The documentation should include the following information:

- Criteria for the diagnosis of osteoporosis, and
- History of treatment as related to progression of disease and ongoing risk factors, and
- Description of treatment failure, or contraindication, or adverse side effects of oral or self administered drugs for osteoporosis as applicable to the patient that supports monoclonal antibodies via SQ injection therapy in lieu of standard oral treatment protocol.

**Denosumab** (Prolia® and Xgeva®) binds to RANKL, a transmembrane of soluble protein essential for the formation, function, and survival of osteoclasts, the cells responsible for bone resorption. Denosumab prevents RANKL from activating its receptor, RANK, on the surface of osteoclasts and their precursors. Prevention of the RANKL/RANK interaction inhibits osteoclast formation, function, and survival, thereby decreasing bone resorption and increasing bone mass and strength in both cortical and trabecular bone.

**Prolia®** (denosumab) is a human IgG2 monoclonal antibody with affinity and specificity for human RANKL (receptor activator of nuclear factor kappa – B ligand). It is produced in genetically engineered mammalian (Chinese hamster ovary) cells.

**Xgeva®** (denosumab) is a human IgG2 monoclonal antibody that binds to human RANKL that is produced in genetically engineered mammalian (Chinese hamster ovary) cells.

**FDA indications for Prolia®:**
- 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 bone loss in men at high risk for fracture receiving androgen deprivation therapy for nonmetastatic prostate cancer
- Treatment of bone loss in women at high risk for fracture receiving adjuvant aromatase inhibitor therapy for breast cancer

*High risk for fracture is defined as a history of osteoporotic fracture; or multiple risk factors for fracture; or patients who failed or are intolerant of other available osteoporosis therapy.

**FDA indication for Xgeva®:**
- Prevention of skeletal–related events in patients with bone metastasis 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

**Limitations:**
Combination use of a bisphosphonate and a monoclonal antibody for the treatment of osteoporosis during an episode of care is not considered reasonable and necessary, and therefore, is not allowed. Combination use of IV and/or oral forms of bisphosphonate therapy as treatment for osteoporosis during an episode of care is not covered. An episode of care includes the duration and frequency of the IV drugs in accordance with FDA labels.

Hypocalcemia, hypovitaminosis D, and other disturbances of bone and mineral metabolism must be effectively treated before starting therapy. Patients must receive supplemental calcium and vitamin D.

The optimal duration of the use of the drugs listed in this LCD has not been determined. It is expected that treatment with these drugs in a Medicare beneficiary meets the evidence-based peer reviewed literature and standards of care in the medical community.

Boniva® is available in oral and IV forms. The IV form will be considered reasonable and necessary only for patients for whom oral therapy cannot be tolerated.

Boniva® Injection is contraindicated for the following conditions:
- Severe renal impairment defined as patients with serum creatinine >200µmol/L [2.3 mg/dL] or creatinine clearance measured or estimated <30 mL/min
- Known hypersensitivity to Boniva® injections or to any of its excipients
- Uncorrected hypocalcemia

Aredia is contraindicated for the following:
- Aredia is contraindicated in patients with clinically significant hypersensitivity to Aredia or other bisphosphonates.
- Pregnancy and lactation

Reclast® used for prevention without a confirmed diagnosis of osteoporosis in postmenopausal women will not be covered because it is not considered medically reasonable and necessary in the diagnosis and treatment of a specific illness or injury as defined in the Social Security Act, Section 1862(a)(1)(A) and as stated in CMS Publication 100-02, Medicare Benefit Policy Manual, chapter 15, section 50.4

Reclast® is contraindicated in the following conditions:
- Hypocalcemia
- Hypersensitivity to the active substance (zoledronic acid) or to any of the excipients
- Pregnancy and lactation
- Patients receiving Zometa®
- Severe renal impairment defined as patients with serum creatinine clearance measured or estimated <35 mL/min

Zometa® is contraindicated for the following conditions:
- Hypersensitivity to zoledronic acid or any component of Zometa®
- Pregnancy and lactation
- Patients receiving Reclast®

Prolia® is contraindicated for the following condition:
- Hypocalcemia
- Patients receiving Xgeva

Xgeva® is not indicated for the following indication:
- Prevention of skeletal related events in patients with multiple myeloma and other cancers of the blood
Xgeva® is contraindicated for the following conditions:

- Hypocalcemia
- Hypersensitivity to Xgeva
- Patients receiving Prolia

**Type of Bill Code**

13x Hospital outpatient
21x Skilled Nursing – inpatient (including Medicare Part A)
75x Clinic – Comprehensive Outpatient Rehabilitation Facility (CORF)
85x Critical Access Hospital

**Revenue Codes**

0636 Pharmacy – Drugs Requiring Detailed Coding

**CPT/HCPCS Codes**

J0897 Injection, Denosumab, 1 mg (Prolia and Xgeva)
J1740 Injection, ibandronate sodium
J2430 Injection, pamidronate disodium, per 30 mg
J3489 Injection, zoledronic acid, 1 mg (Reclast and Zometa)

**ICD-10 Codes that Support Medical Necessity**

**Group 1 Paragraph: HCPCS Code J0897 (Prolia®)**

**Group 1 Codes:**

<table>
<thead>
<tr>
<th>Code Range</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>M80.00XA - M80.88XS</td>
<td>Osteoporosis with current pathological fracture</td>
</tr>
<tr>
<td>M81.0</td>
<td>Age-related osteoporosis without current pathological fracture</td>
</tr>
<tr>
<td>M81.6</td>
<td>Localized osteoporosis [Lequesne]</td>
</tr>
<tr>
<td>M81.8</td>
<td>Other osteoporosis without current pathological fracture</td>
</tr>
<tr>
<td>M85.80-M85.9</td>
<td>Other specified disorders of bone density and structure, unspecified site – Disorder of bone density and structure, unspecified</td>
</tr>
</tbody>
</table>

**Group 2 Paragraph: HCPCS Code J0897 (Prolia®) for treatment of bone loss in women at high risk for fracture receiving adjuvant aromatase inhibitor therapy for breast cancer, ICD-10-CM M85.80-M85.9 is reported with ICD-10-CM code Z85.3 and Z79.811.**

**Group 2 Codes:**

<table>
<thead>
<tr>
<th>Code</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Z85.3</td>
<td>Personal history of malignant neoplasm of breast</td>
</tr>
<tr>
<td>Z79.811</td>
<td>Long term (current) use of aromatase inhibitors</td>
</tr>
</tbody>
</table>

**Group 3 Paragraph: HCPCS Code J0897 (Prolia®): For treatment of bone loss in men at high risk for fracture receiving androgen deprivation therapy for nonmetastatic prostate cancer, ICD-10-CM code M85.80-M85.9 is reported with ICD-10-CM code Z85.46 and Z79.899.**
### Group 3 Codes:

<table>
<thead>
<tr>
<th>Code</th>
<th>Description</th>
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</thead>
<tbody>
<tr>
<td>Z85.46</td>
<td>Personal history of malignant neoplasm of prostate</td>
</tr>
<tr>
<td>Z79.899</td>
<td>Other long term (current) drug Therapy</td>
</tr>
</tbody>
</table>

### Group 4 Paragraph: HCPCS Code J0897 (Xgeva®)

### Group 4 Codes:

<table>
<thead>
<tr>
<th>Code</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>C79.51-C79.52</td>
<td>Secondary malignant neoplasm of bone and bone marrow</td>
</tr>
<tr>
<td>D48.0</td>
<td>Neoplasm of uncertain behavior of bone and articular cartilage</td>
</tr>
<tr>
<td>E83.52</td>
<td>Hypercalcemia (associated with malignancy)</td>
</tr>
</tbody>
</table>

### Group 5 Paragraph: HCPCS Code J1740 (Boniva®)

### Group 5 Codes:

<table>
<thead>
<tr>
<th>Code</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>C79.51</td>
<td>Secondary malignant neoplasm of bone</td>
</tr>
<tr>
<td>C79.52</td>
<td>Secondary malignant neoplasm of bone marrow</td>
</tr>
<tr>
<td>M80.00XA-M80.88XS</td>
<td>Osteoporosis with current pathological fracture</td>
</tr>
<tr>
<td>M81.0</td>
<td>Age-related osteoporosis without current pathological fracture</td>
</tr>
<tr>
<td>M81.6</td>
<td>Localized osteoporosis [Lequesne]</td>
</tr>
<tr>
<td>M81.8</td>
<td>Other osteoporosis without current pathological fracture</td>
</tr>
<tr>
<td>M88.0-M88.9</td>
<td>Osteitis deformans [Paget’s disease of bone]</td>
</tr>
<tr>
<td>T38.0X5A-T38.0X5S</td>
<td>Adverse effect of glucocorticoids and synthetic analogues</td>
</tr>
<tr>
<td>T50.0X5A-T50.0X5S</td>
<td>Adverse effect of mineralocorticoids and their antagonists</td>
</tr>
</tbody>
</table>

### Group 6 Paragraph: HCPCS Code J2430 (Aredia®)

### Group 6 Codes:

<table>
<thead>
<tr>
<th>Code</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>C50.011-C50.929*</td>
<td>Malignant neoplasms of breast</td>
</tr>
<tr>
<td>C79.51-C79.52*</td>
<td>Secondary malignant neoplasm of bone and bone marrow</td>
</tr>
<tr>
<td>C90.00-C90.02</td>
<td>Multiple myeloma</td>
</tr>
<tr>
<td>E83.52</td>
<td>Hypercalcemia (associated with malignancy)</td>
</tr>
<tr>
<td>M81.0</td>
<td>Age-related osteoporosis without current pathological fracture</td>
</tr>
<tr>
<td>M81.6</td>
<td>Localized osteoporosis [Lequesne]</td>
</tr>
<tr>
<td>M81.8</td>
<td>Other osteoporosis without current pathological fracture</td>
</tr>
<tr>
<td>M88.0-M88.9</td>
<td>Osteitis deformans [Paget’s disease of bone]</td>
</tr>
<tr>
<td>Z85.3*</td>
<td>Personal history of malignant neoplasm of breast</td>
</tr>
</tbody>
</table>

**NOTE:** The billing of Pamidronate for osteolytic bone metastases of breast cancer requires a dual diagnosis. ICD-10-CM code C79.51 or C79.52 must be billed with the related neoplasm code (C50.011-C50.929, or Z85.3). The starred (*) ICD-10-CM codes listed above may NOT be billed alone.

### Group 7 Paragraph: HCPCS Code J3489 (Zometa®)

### Group 7 Codes: group 2

<table>
<thead>
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<th>Code</th>
<th>Description</th>
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</thead>
<tbody>
<tr>
<td>C79.51-C79.52</td>
<td>Secondary malignant neoplasm of bone and bone marrow</td>
</tr>
<tr>
<td>C90.00-C90.02</td>
<td>Multiple myeloma</td>
</tr>
<tr>
<td>E83.52</td>
<td>Hypercalcemia (associated with malignancy)</td>
</tr>
<tr>
<td>M89.9</td>
<td>Disorder of bone, unspecified</td>
</tr>
</tbody>
</table>
Bisphosphonates (Intravenous [IV]) and Monoclonal Antibodies in the Treatment of Osteoporosis and Their Other Indications

<table>
<thead>
<tr>
<th>Code</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>M94.9</td>
<td>Disorder of cartilage, unspecified</td>
</tr>
</tbody>
</table>

**Group 8 Paragraph: HCPCS Code J3489 (Reclast®)**

**Group 8 Codes:**

<table>
<thead>
<tr>
<th>Code</th>
<th>Description</th>
</tr>
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<tbody>
<tr>
<td>M81.0</td>
<td>Age-related osteoporosis without current pathological fracture</td>
</tr>
<tr>
<td>M81.6</td>
<td>Localized osteoporosis [Lequesne]</td>
</tr>
<tr>
<td>M81.8</td>
<td>Other osteoporosis without current pathological fracture</td>
</tr>
<tr>
<td>M88.0-M88.9</td>
<td>Osteitis deformans [Paget's disease of bone]</td>
</tr>
<tr>
<td>T38.0X5A-T38.0X5S</td>
<td>Adverse effect of glucocorticoids and synthetic analogues</td>
</tr>
<tr>
<td>T50.0X5A-T50.0X5S</td>
<td>Adverse effect of mineralocorticoids and their antagonists</td>
</tr>
</tbody>
</table>

**Diagnoses that Support Medical Necessity**

N/A

**ICD-10 Codes that DO NOT Support Medical Necessity**

N/A

**Diagnoses that DO NOT Support Medical Necessity**

N/A

**Associated Information**

**Documentation Requirements**

Medical record documentation must be maintained by the ordering/referring physician or the nonphysician practitioner and should include the following, and be available to Medicare upon request:

- The record must demonstrate the medical need for the use of the drug by clearly indicating the condition for which the drug is being used.
- The medical record must indicate that the treatment is based on diagnostic information and lab work completed to confirm the indications for use of the drug.
- The specific signs and symptoms must be documented to substantiate the FDA labeled or the FDA off labeled indications for the drug usage.
- For the osteoporosis indications for the drugs outlined in this LCD, the medical record must indicate that the patient has been examined for secondary causes of osteoporosis.
- An indication that the patient has been advised to take adequate calcium and vitamin D supplementation.
- For the osteoporosis indications for the drugs outlined in this LCD, an indication that the patient has been advised to practice regular weight bearing and muscle strengthening exercise to reduce risk of falls and fracture, and to avoid tobacco smoking and excessive alcohol intake.
- The medication administration record (MAR) including the name, date, time, route and dose of the drug administered to the patient.
- A statement that demonstrates oral health was discussed with the patient.

This documentation is usually found in the history and physical and/or in the office/progress notes of the medical record. In addition, the MAR should be included indicating the name, date, time, route and amount of drug administered. The physician order should also be included.

**In addition, specific documentation for each drug is also required as outlined below:**
Bisphosphonate therapy:

The following bisphosphonate injections (administered IV) are considered medically reasonable and necessary when administered as outlined in this LCD. The coverage of IV bisphosphonates must be supported in the medical record. The documentation should include the following information:

- Criteria for the diagnosis of osteoporosis, and
- History of treatment as related to progression of disease and ongoing risk factors, and
- Description of treatment failure of oral or self-administered drugs for osteoporosis as applicable to the patient that supports IV therapy in lieu of standard oral treatment protocol.
- An indication that the serum creatinine was measured prior to the administration of the drug.
- An indication that the oral health of the patient was discussed.

Boniva®

The documentation must clearly state why IV Boniva® is being given as opposed to the oral form of the drug. Documentation should demonstrate if one of the following apply:

- Patient has a diagnosis of esophageal stricture, achalasia, or other severe esophageal dysmotility disorder; OR
- Patient has a history of severe malabsorption making use of oral bisphosphonates ineffective; OR
- Patient has an inability to stand or sit upright for 60 minutes; OR
- Patient had adverse side effects secondary to the oral form of the drug that required the withdrawal of the oral form of the medication.
- An indication that the serum creatinine was measured before Boniva® was administered
- An indication that the patient does not have severe renal impairment (patients with severe renal impairment with serum creatinine >200 µmol/L [2.3 mg/dL] or creatinine clearance measured or estimated <30 mL/min should not receive Boniva® injection)
- Documentation to support that the drug was administered per IV route by a healthcare professional with a 3mg/3 mL bolus over 15 to 30 seconds every three months

Aredia®

- Patients who receive Aredia should have serum creatinine assessed prior to each treatment.
- Serum calcium, electrolytes, phosphate, magnesium, and CBC, differential, and hematocrit/hemoglobin must be closely monitored in patients treated with Aredia.
- Patients who have preexisting anemia, leukopenia, or thrombocytopenia should be monitored carefully in the first 2 weeks following treatment

Aredia for Hypercalcemia of Malignancy

- Intravenous infusion, 60mg – 90mg given as a single-dose over 2 to 24 hours for moderate hypercalcemia; and intravenous infusion, 90mg given as a single-dose over 2 to 24 hours for severe hypercalcemia.

Aredia for Moderate to Severe Paget’s Disease of Bone

- Intravenous infusion, 30mg daily over 4 hours, on 3 consecutive days for a total dose of 90mg. Osteolytic Bone Lesions of Multiple Myeloma – intravenous infusion, 90mg over 4 hours given on a monthly basis.

Aredia for Osteolytic Bone Metastases of Breast Cancer

- Intravenous infusion, 90mg over 2 hours given every 3-4 weeks.
- Patients treated with Aredia for bone metastases should have the dose withheld if renal function has deteriorated.
Reclast® - All Patients

- An indication that the patient received adequate hydration prior to treatment
- An indication that the patient has a creatinine clearance of ≥35 mL/min or better
- Documentation to support that the drug was administered one time in a year per IV route by a healthcare professional with 5 mg Reclast® infused IV over no less than 15 minutes given over a constant infusion rate with a 10 mL normal saline flush of the IV line following the infusion

Reclast® for Glucocorticoid-Induced Osteoporosis in Men and Women (must meet above criteria also)

- An indication that the patient is either initiating or continuing to take system glucocorticoids in a daily dosage of 7.5 mg or greater of prednisone and who are expected to remain on glucocorticoids for at least 12 months
- An indication that the patient is taking at least 1200 mg calcium and 800-1000 IU vitamin D per day

Reclast® for Women or Men with Osteoporosis

- An indication that the patient is taking at least 1200 mg calcium and 800-1000 IU vitamin D per day

Reclast® for Paget’s Disease

- An indication that the patient has been instructed to take 1500 mg elemental calcium daily in divided doses (750 mg two times per day, or 500 mg three times per day) and 800 IU vitamin D per day, particularly in the 2 weeks following the administration of Reclast®
- An indication that the patient has one of the following:
  - An elevated serum alkaline phosphatase of two times or higher than the upper limit of the age-specific normal reference range, or
  - The patient is symptomatic, or
  - The patient is at risk for complications from the disease, to induce remission (normalization of serum alkaline phosphotase) prior to treatment with Reclast®

Reclast® for Re-Treatment of Paget’s Disease

- An indication that the patient is experiencing a relapse based on serum alkaline phosphatase, or
- An indication that the patient has failed to achieve normalization of their serum alkaline phosphatase, or
- An indication that the patient has symptoms as dictated by current standard medical practice.

Zometa®

- An indication that the patient is not on any other bisphosphonate medication(s)
- Documentation to support that the drug was administered per IV route by a healthcare professional with a dosage amount not exceeding 4 mg administered for no less than 15 minutes
- An indication that the renal status of the patient has been monitored
- Retreatment with Zometa® 4 mg may be considered if serum calcium does not return to normal or remain normal after treatment.
- It is recommended that a minimum of 7 days elapse before re-treatment to allow for full response to the initial dose

Zometa® for Hypercalcemia of Malignancy

- An indication that the patient has an albumin-corrected serum calcium of ≥ 12 mg/dL (3.0 mmol/L)
- The date of the last treatment must be indicated

Zometa® for Multiple Myeloma and Metastatic Bone Lesions of Solid Tumors
Bisphosphonates (Intravenous [IV]) and Monoclonal Antibodies in the Treatment of Osteoporosis and Their Other Indications. A/B

- An indication that for the patient with a creatinine clearance of > 60 mL/min, a 4 mg IV infusion over no less than 15 minutes was administered every 3-4 weeks by a healthcare provider
- An indication that the patient was coadministered oral calcium supplements of 500 mg and a multiple vitamin containing 400 IU of vitamin D per day

Monoclonal Antibodies

Prolia®

Prolia All Patients
- An indication that the serum creatinine was measured prior to the administration of the drug.
- An indication that the oral health of the patient was discussed
- An indication that the patient received a single dose of 60 mg SQ Prolia® which was administered by a healthcare professional into the upper arm, the upper thigh or the abdomen once in 6 months
- An indication that the patient was instructed to take 1000 mg of calcium and at least 400 IU of vitamin D per day

Prolia® for Men and Postmenopausal Women with Osteoporosis
- Criteria for the diagnosis of osteoporosis, and
- History of treatment as related to progression of disease and ongoing risk factors, and
- Description of treatment failure of oral or self-administered drugs for osteoporosis as applicable to the patient that supports IV therapy in lieu of standard oral treatment protocol.
- An indication that the patient meets the definition of osteoporosis with high risk for fracture, or
- An indication that the patient has failed or is intolerant of other available osteoporotic therapy

Prolia® for Treatment of Bone Loss in Women Receiving Adjuvant Aromatase Inhibitor Therapy for Breast Cancer
- An indication that the patient is a woman receiving adjuvant aromatase inhibitor therapy for breast cancer

Prolia® for Treatment of Bone Loss in Men Receiving Androgen Deprivation Therapy for Nonmetastatic Prostate Cancer
- An indication that the patient is a man receiving androgen deprivation therapy for prostate cancer

Xgeva® all patients
- An indication that the patient is taking calcium and vitamin D supplements as necessary to treat or prevent hypocalcemia
- An indication Xgeva® was administered by a healthcare professional into the upper arm, the upper thigh or the abdomen

Xgeva® for the prevention of skeletal-related events in patients with bone metastasis from solid tumors
- An indication that the patient received a single dose of 120 mg SQ Xgeva®.

Xgeva® 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
- An indication that the patient received a single dose of 120 mg SQ Xgeva® every 4 weeks with additional 120 mg doses on days 8 and 15 of the first month of therapy

Xgeva® for the prevention of skeletal-related events in patients with bone metastasis from solid tumors
- An indication that the patient received a single dose of 120 mg SQ Xgeva® every 4 weeks with additional 120 mg doses on days 8 and 15 of the first month of therapy
Utilization Guidelines

It is expected that these services would be performed as indicated by current literature and/or standards of practice and should follow the guidelines for administration and safety found in the FDA approved labels for these drugs. When services are performed in excess of established parameters, they may be subject to medical review for medical necessity. Utilization guidelines and expected documentation requirements in support of such, are stated in the “Documentation Requirements” section of this LCD.

Sources of Information and Basis for Decision

FCSO reference LCD number(s) – L32100


Pharmacy and Therapeutics, 29, 431-436. Blackwell Publishing Ltd.


Prolia® (denosumab) prescribing information. (2011). Amgen, Inc

Bisphosphonates (Intravenous [IV]) and Monoclonal Antibodies in the Treatment of Osteoporosis and Their Other Indications. A/B


Xgeva™ (denosumab) prescribing information. (2010). Amgen, Inc.


**Start Date of Comment Period**

N/A

**End Date of Comment Period**

N/A

**Start Date of Notice Period**

04/01/2014

**Revision History**

**Revision History Number: R3**

**Revision Number: 3**
Publication: October 2016 Connection
LCR A/B2016-102

Explanation of Revision: The LCD was revised to remove ICD-10 diagnosis codes M89.9 and M94.9 and replace with the diagnosis code range M85.80-M85.9 in the “ICD-10 Codes that Support Medical Necessity” section of the LCD for HCPCS code J0897 (Prolia®). The effective date of this revision is based on date of service.

**Revision History Number: R2**

**Revision Number: 2**
Publication: March 2016 Connection
LCR A/B2016-050

Explanation of Revision: The LCD was revised to change ICD-10 diagnosis code range M88.1-M88.9 to ICD-10 diagnosis code range M88.0-M88.9 in the “ICD-10 Codes that Support Medical Necessity” section of the LCD for HCPCS code J3489 (Reclast®). The effective date of this revision is for claims processed on or after 03/10/2016, for dates of service on or after 10/01/15.

**Revision History Number: R1**

**Revision Number: 1**
Publication: February 2016 Connection
LCR A/B2016-039
Explanation of Revision: The LCD was revised to add ICD-10-CM diagnosis code range M80.00XA-M80.88XS to the “ICD-10 Codes that Support Medical Necessity” section of the LCD for HCPCS code J0897 (Prolia®). In addition, the asterisked statement under the “ICD-10 Codes that Support Medical Necessity” section of the LCD was removed for HCPCS codes J1740 (Boniva®) and J3489 (Reclast®), as this information pertains to coding and can be found the ICD-10-CM codebook. The effective date of this revision is for claims processed on or after 02/08/16, for dates of service on or after 10/01/15.

**Revision Number:** Original

This LCD replaces all previous LCD versions (refer to “Sources of Information and Basis for Decision” section of the LCD) and publications on this subject to comply with ICD-10-CM based on Change Request 8112. The effective date of this LCD is based on date of service.

**Related Documents**

N/A

**LCD Attachments**

Coding Guidelines

Document formatted: 10/03/2016 (SW/et)