Clinical Policy Title: Agents for osteoporosis

Clinical Policy Number: 00.02.05

Effective Date: March 1, 2014
Initial Review Date: December 18, 2013
Most Recent Review Date: January 11, 2018
Next Review Date: January 2019

Related policies:

CP# 236.200 PerformRx Injectable-Infusible Osteoporosis Agents
CP# 17.01.01 Bone mineral density measurement

ABOUT THIS POLICY: AmeriHealth Caritas has developed clinical policies to assist with making coverage determinations. AmeriHealth Caritas’ clinical policies are based on guidelines from established industry sources, such as the Centers for Medicare & Medicaid Services (CMS), state regulatory agencies, the American Medical Association (AMA), medical specialty professional societies, and peer-reviewed professional literature. These clinical policies along with other sources, such as plan benefits and state and federal laws and regulatory requirements, including any state- or plan-specific definition of “medically necessary,” and the specific facts of the particular situation are considered by AmeriHealth Caritas when making coverage determinations. In the event of conflict between this clinical policy and plan benefits and/or state or federal laws and/or regulatory requirements, the plan benefits and/or state and federal laws and/or regulatory requirements shall control. AmeriHealth Caritas’ clinical policies are for informational purposes only and not intended as medical advice or to direct treatment. Physicians and other health care providers are solely responsible for the treatment decisions for their patients. AmeriHealth Caritas’ clinical policies are reflective of evidence-based medicine at the time of review. As medical science evolves, AmeriHealth Caritas will update its clinical policies as necessary. AmeriHealth Caritas’ clinical policies are not guarantees of payment.

Coverage policy

AmeriHealth Caritas considers the use of the following agents for treatment of osteoporosis to be clinically proven and, therefore, medically necessary:

- BONIVA INJECTION® (ibandronate sodium): 3 mg/3 mL single use syringe.
- FORTEO® (teriparatide [rDNA origin] injection): 20 mcg/dose in a 2.4 mL prefilled pen.
- PROLIA™ (denosumab): 60 mg/1 mL.
- RECLAST® (zoledronic acid): 5 mg/100 mL (Watts, 2012; Qaseem, 2017).

Dosage and administration:

Boniva - Osteoporosis in Postmenopausal Women: 3 mg IV given once every three months.
Forteo - Osteoporosis in Postmenopausal Women/Men & Treatment and Prevention of Glucocorticoid-Induced Osteoporosis: 20 mcg once a day administered as a subcutaneous injection into the thigh or abdominal wall. The length of therapy should be no longer than two years.

Prolia - Osteoporosis in Men & Postmenopausal Women, Bone Loss in Men Receiving Androgen Deprivation Therapy for Prostate Cancer & Bone Loss in Women Receiving Adjuvant Aromatase Inhibitor Therapy for Breast Cancer: 60 mg administered as a single subcutaneous injection once every six months administered via subcutaneous injection in the upper arm, the upper thigh, or the abdomen. All patients should receive calcium 1,000 mg daily and at least 400 IU vitamin D daily.

Reclast - Treatment of Postmenopausal Osteoporosis/Osteoporosis in Men & the Treatment and Prevention of Glucocorticoid-Induced Osteoporosis: 5 mg infusion once a year given intravenously over no less than 15 minutes. Patients must be adequately supplemented with calcium and vitamin D if dietary intake is not sufficient. All patients should receive at least 1,200 mg of calcium and 800–1,000 IU of vitamin D daily.

Prevention of Osteoporosis in Postmenopausal Women: a 5 mg infusion given once every two years intravenously over no less than 15 minutes. Patients must be adequately supplemented with calcium and vitamin D if dietary intake is not sufficient. Postmenopausal women require an average of 1,200 mg calcium and 800–1,000 IU vitamin D daily.

The AmeriHealth Caritas PerformRxSM policy for administering the four agents for osteoporosis is given as Appendix 1.

Limitations:

None.

Alternative covered services:

Medications approved for osteoporosis that are prescribed not by infusion but by other routes:

1. Alendronate sodium or alendronate sodium plus vitamin D3 (Fosamax®/Fosamax Plus D) - tablet.
2. Ibandronate 150 mg tablet.
3. Risedronate sodium or risedronate sodium with calcium carbonate (Actonel®, Actonel® with Calcium and Atelvia™) - tablet.
4. Calcitonin-salmon (Fortical® and Miacalcin®) - nasal spray.
5. Raloxifene (Evista®) - tablet.
6. Estrogen therapy (ET) and hormone therapy (HT) (multiple brands available) - tablet or skin (transdermal) patch.
Bisphosphonates: A class of drugs approved for the prevention or treatment of osteoporosis. These medications reduce the activity of cells that cause bone loss.

Parathyroid hormone: A form of human parathyroid hormone approved for postmenopausal women and men with osteoporosis who are at high risk for having a fracture. Use of the drug for more than two years is not recommended.

RANK ligand inhibitor: A protein that is approved for postmenopausal women with osteoporosis who are at high risk for fracture.

Estrogen agonists/antagonists: Also called a selective estrogen receptor modulator, approved for the prevention and treatment of osteoporosis in postmenopausal women. These drugs are not estrogens, but they have estrogen-like effects on some tissues and estrogen-blocking effects on other tissues.

Calcitonin: A hormone approved for the treatment of osteoporosis in women who are at least five years beyond menopause. Calcitonin is involved in calcium regulation and bone metabolism.

Estrogen and hormone therapy: Estrogen and combined estrogen and progestin (hormone therapy) are approved for the prevention of postmenopausal osteoporosis as well as the treatment of moderate to severe hot flashes and vaginal dryness that may accompany menopause. Estrogen without an added progestin is recommended only for women who have had a hysterectomy (surgery to remove the uterus), because estrogen increases the risk of developing cancer of the uterine lining and progestin reduces that risk.

Background

Osteoporosis is a progressive bone disease characterized by a decrease in bone mass and density which can lead to an increased risk of fracture. In osteoporosis, the bone mineral density is reduced, bone microarchitecture deteriorates, and the amount and variety of proteins in bone are altered. Osteoporosis is defined by the World Health Organization (WHO) as a basis for assessing fracture risk in screening. The definition, based on recommendations of expert panels convened in 1994 and 2008, combines bone mineral density (T-score) and history of a fracture (4BoneHealth, 2016).

In the United States, of 99 million persons age 50 and older, over half have either osteoporosis or low bone mass. A total of 10.2 million had osteoporosis, while another 43.4 million had low bone mass in 2010. Women represented 80 percent (8.2 million) of persons with osteoporosis and 63 percent (27.3 million) of men with low bone mass. The total of over 53.6 million Americans over age 50 with either disorder in 2010 is expected to rise to over 70 million by 2030. Non-Hispanic whites had the highest rate of these conditions, while non-Hispanic blacks had the lowest (Wright, 2014).

The form of osteoporosis most common in women after menopause is referred to as primary type 1 or postmenopausal osteoporosis. Primary type 2 osteoporosis or senile osteoporosis occurs after age 75
and is seen in females and males at a ratio of 2:1. Secondary osteoporosis may arise at any age and affect men and women equally. This form results from chronic predisposing medical problems or disease or prolonged use of medications such as glucocorticoids, when the disease is called steroid- or glucocorticoid-induced osteoporosis.

Perhaps the greatest threat posed by osteoporosis is the elevated risk of fractures. Over 80 percent of fractures in persons over age 50 are caused by osteoporosis. Hip fractures are among the most common types of fractures in the elderly; they are not only costly, but hazardous. Among elderly women who suffer a broken hip, the mortality rate in the next year is twice that of other women the same age, 16.9 versus 8.4 percent (LeBlanc, 2011).

Effective diagnosis and treatment of osteoporosis can prevent millions of fractures and the pain and disability that follow them. However, many fractures still occur despite preventive efforts. For fragile patients with severe osteoporosis, slowing bone loss with anti-resorptive drugs may be insufficient to protect against fracture. An anabolic agent that increases bone formation can represent a more effective option. Currently, teriparatide is one U.S. Food and Drug Administration (FDA) approved bone anabolic for treatment of osteoporosis.

Screening for osteoporosis is covered under the Patient Protection and Affordable Care Act of 2010. For persons with a new insurance plan starting September 23, 2010, this screening is covered without a copayment or coinsurance to meet a deductible (HHS, 2010). A number of states have enacted laws addressing education, public awareness, and prevention of osteoporosis; some mandate insurance coverage for osteoporosis-related diagnostic and treatment services.

A 2012 guideline from the Endocrine Society sets recommendations for initial screening (using dual energy X-ray and absorbiometry) and follow-up of bone mineral density in males over 50, and also states that pharmacological therapy is indicated for those with low density or other risk factors for fracture (Watts, 2012). The U.S. Preventive Services Task Force cited evidence that drug therapy reduces fracture risk in elderly women as part of its guideline on screening (USPSTF, 2011).

The American College of Rheumatology recommends adults with glucocorticoid-induced osteoporosis at moderate-to-high risk for fracture be treated with calcium and vitamin D, plus an additional osteoporosis medication — preferably an oral bisphosphonate (Buckley, 2017). The latest update of the American College of Physicians guideline recommends that clinicians offer pharmacologic treatment with alendronate, riserdronate, zoledronic acid, or denosumab to reduce the risk for hip and vertebral fractures in women who have known osteoporosis, for five years (Qaseem, 2017). The UK National Osteoporosis Guideline Group also produced a guideline update in 2017, recommending the same four drugs for women at risk, along with specific doses and intervals of administration (Compston, 2017).

Although there is no cure for osteoporosis, it is treatable and preventable. Several medications are available to help stop or slow bone loss, to help form new bone, and to reduce the risk of fractures. Among the non-nitrogen-containing bisphosphonates, there are three main alternatives: clodronate,
etidronate, and tiludronate. Among the nitrogen-containing bisphosphonates, aside from ibandronate, there are six basic alternatives: alendronate, neridronate, olpadronate, pamidronate, risedronate, and zoledronate. The bisphosphonates available in an IV formulation include ibandronate, pamidronate, and zoledronate. However, only ibandronate IV is approved for the treatment of postmenopausal osteoporosis; the other IV formulations are used for the treatment of cancer patients. Other clinical alternatives include the following: calcium and vitamin D supplementation; calcitonin, a naturally occurring hormone involved in calcium regulation and bone metabolism; estrogen/progestin therapy; raloxifene, a selective estrogen receptor modulator; teriparatide, an injectable form of human parathyroid hormone; and combination therapy.

**Searches**

AmeriHealth Caritas searched PubMed and the databases of:
- UK National Health Services Centre for Reviews and Dissemination.
- Agency for Healthcare Research and Quality’s National Guideline Clearinghouse and other evidence-based practice centers.
- The Centers for Medicare & Medicaid Services (CMS).

Searches were conducted on November 15, 2017. Search terms were: “osteoporosis” and “bisphosphonates.”

We included:
- **Systematic reviews**, which pool results from multiple studies to achieve larger sample sizes and greater precision of effect estimation than in smaller primary studies. Systematic reviews use predetermined transparent methods to minimize bias, effectively treating the review as a scientific endeavor, and are thus rated highest in evidence-grading hierarchies.
- **Guidelines based on systematic reviews**.
- **Economic analyses**, such as cost-effectiveness, and benefit or utility studies (but not simple cost studies), reporting both costs and outcomes — sometimes referred to as efficiency studies — which also rank near the top of evidence hierarchies.

**Findings**

Few studies have compared efficacy of medications for osteoporosis against each other. The Agency for Healthcare Research and Quality reports that alendronate, risedronate, zoledronic acid, denosumab, and teriparatide reduce risk of vertebral and non-vertebral fractures among postmenopausal women with the disorder. The same drugs (minus teriparatide) also show significant results in preventing hip fractures among postmenopausal women with osteoporosis (Crandall, 2012).

Findings to date have found all bisphosphonates to be effective in reducing fracture risk, with zoledronic acid typically cited as most effective. These studies include:
• A meta-analysis of nine controlled trials with 2,464 men with osteoporosis found that compared to placebo, bisphosphonates reduced risk of vertebral and non-vertebral fracture by 64 percent and 48 percent, respectively (Chen, 2015a).
• Guidelines published by the French National Authority for Health in 2012 recommended pharmacotherapy for women with a history of severe osteoporotic fracture, with zoledronic acid as the preferred first-line medication after a hip fracture (Briot, 2012).
• In a meta-analysis of eight placebo-controlled trials, zoledronic acid also was found to be more effective than four other drug therapies in reducing vertebral, non-vertebral, and hip fractures among postmenopausal women with osteoporosis (Jansen, 2011).
• A meta-analysis of 10 trials ranked zoledronic acid as most effective in preventing vertebral fracture in primary osteoporosis, while risedronate was most effective in preventing fractures in primary and corticosteroid-induced osteoporosis (Zhou, 2016a).
• A meta-analysis of 36 studies of persons taking a bisphosphonate for primary osteoporosis documented that all seven drugs caused significant decreases in fracture risk compared to placebo, with zoledronic acid having the greatest decrease (Zhou, 2016b).
• A systematic review of 30 studies including 59,209 postmenopausal women taking one of nine drugs assessed fracture rates, including vertebral, non-vertebral, hip, and wrist fractures. Teriparatide, zoledronic acid, and denosumab demonstrated the greatest efficacy in preventing non-vertebral and vertebral fractures (Hopkins, 2011).
• A systematic review and meta-analysis of 22 studies (n=4,868) documented that males had a significantly lower risk of vertebral fractures (relative risk = 0.368) and non-vertebral fractures (0.604), compared to controls. Significantly lower risk of vertebral fractures was observed with alendronate (0.328) and risedronate (0.428), but insignificantly lower risk with calcitonin (RR = 0.272) and denosumab (RR=0.256) (Nayak, 2017).
• A meta-analysis of 42 studies (n=92,904) compared 10 drugs — including all four covered in this policy, except teriparatide — in their ability to prevent vertical fractures in women with postmenopausal osteoporosis. In prevention of new fractures, all 10 were more effective than placebo, with etidronate most effective with a 76 percent reduction. Zoledronic acid and parathyroid hormone were more effective than other drugs. For preventing clinical fractures, zoledronic acid was most effective (75 percent reduction) and denosumab proved a desirable second option (52 percent reduction) (Wang G, 2017).
• A meta-analysis of six trials (n=618) found that teriparatide was associated with greater density in the lumbar spine (p<0.0001) and femoral neck (p<0.04) compared to alendronate, 6 to 18 months after treatment, but there were no differences between the two drugs in reducing fracture risk (Wang YK, 2017).

Other studies of osteoporosis drug efficacy have focused on outcomes other than fracture risk. A meta-analysis of 13 studies and 3,647 men with osteoporosis taking one of eight drugs (compared to placebo) documented that each drug improved bone mass density, and that zoledronate was the most effective (Chen, 2015a).
A meta-analysis assessed four studies and 3,088 patients with osteoporosis and a fracture, randomized to taking a bisphosphonate and controls. It found that bisphosphonates caused significant reductions in second hip fractures (40 percent, n=33) and mortality (34 percent, n=122), compared to controls. The overall complication rate in elderly persons taking a bisphosphonate was not increased (Peng, 2016).

A meta-analysis showed the efficacy of bisphosphonates on reducing bone-specific alkaline phosphatase and C-terminal telopeptide of type I collagen, and increasing bone marrow density (Chen, 2015b).

A meta-analysis of 34 studies and 11,090 subjects with osteoporosis and bone mass density treated with ibandronate assessed measures of improvement. The study identified that longer treatment duration (one to five years), increasing age, lower baseline T scores, and higher serum CTX levels were the predictors of the greatest improvements in patient health status (Ma, 2016).

Some studies analyze the adverse effects of bisphosphonates. A Cochrane review of 15 trials (n=1703) of subjects taking bisphosphonates found the cases had a lower rate of serious adverse effects (14.7 percent versus 16.3 percent) than did controls. Withdrawals due to adverse events were similar (7.7 percent and 7.3 percent) (Allen, 2016). A meta-analysis of nine studies (n=4,890) of postmenopausal women compared those taking denosumab and bisphosphonate one to two years after therapy began showed no significant difference in adverse event rates and withdrawals due adverse events between those given denosumab and those taking other bisphosphonates (Beaudoin, 2016).

Some large-scale studies that are not systematic analyses have been published. In a study of 7,868 women ages 60 to 90, denosumab reduced vertebral fractures by 67 percent (2.3 percent versus 7.2 percent) in the following three years (Cummings, 2009). A study of 1,199 men ages 50 to 85 found that zoledronic acid reduced the risk of vertebral fracture by 67 percent, or 1.6 percent versus 4.9 percent (Boonen, 2012).

While osteoporosis is rare in children and adolescents, bisphosphonate therapy is considered the pharmacological treatment of choice (Saraff, 2015). Few studies have evaluated efficacy of this treatment in pediatric populations. One review of 281 children in nine studies found three fractures in those taking a bisphosphonate, versus six in the control group (Ward, 2007). A study of adolescents and young adults (ages 10 to 45) enrolled in a large health insurance company reported the number of bisphosphonates initiators decreased from 1,670 to 344 between 2004 and 2012; authors speculate that growing concerns over side effects may be the cause of this trend (Xie, 2015).

The 2012 Agency for Healthcare Research and Quality review also noted that adherence to drug therapy for osteoporosis is poor due to dosing frequency, side effects, knowledge of osteoporosis, and cost (Crandall, 2012). A systematic review found that over a one-year period, adherence to bisphosphonates in males with osteoporosis ranged from 32 percent to 64 percent, posing a barrier to improving outcomes (Mikyas, 2014). Patients are much more likely to prefer annual zoledronic acid infusions (66.4 percent to 78.8 percent) over weekly bisphosphonates (9.0 percent to 19.7 percent) (Lee, 2011).
Bisphosphonates may have other benefits other than reducing risk from osteoporosis. A 2010 review of 154,768 women, 2,816 using a bisphosphonate at the start of the project, followed subjects for a mean of 7.8 years. Invasive breast cancer incidence and estrogen receptor-positive invasive cancers were significantly lower (-32 percent and -30 percent) for bisphosphonate users (Chlebowski, 2010).

Studies of cost effectiveness of bisphosphonates for osteoporosis have been conducted. One study from Switzerland, consistent with other European studies, found treatment with oral bisphosphonates in women over age 70 with osteoporosis or at least one fracture risk is cost effective relative to no treatment. Results are most affected with changes in fracture risk, cost of fractures, cost of treatment, nursing home admissions, and adherence to treatment (Lippuner, 2011).

There may be disparities among utilization and outcomes for persons with osteoporosis. One study of 48,390 women over age 50 in northern California taking bisphosphonate therapy and tracked for an average of 7.7 years documented fracture risk was eight-fold higher for Asian women than for white women (64.2 versus 7.6 fractures per 100,000). Asian women also were treated an average of 3.8 years, significantly greater than the 2.7 figure for white women (Lo, 2016).

Policy updates:

A total of three guidelines/other and nine peer-reviewed references were added to this policy, while one guideline/other and two peer-reviewed references were removed in 2018.

The December 2016 version of this policy contains seven new guidelines/other, along with 16 peer-reviewed references, including a number of recent meta-analyses and systematic reviews. A number of general or noncurrent references have been removed. The background and findings sections have been rewritten to reflect these new references, and the summary of clinical evidence section now reflects only the most current and most critical results.

Summary of clinical evidence:

<table>
<thead>
<tr>
<th>Citation</th>
<th>Content, Methods, Recommendations</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Peng (2016)</strong></td>
<td><strong>Key points:</strong></td>
</tr>
</tbody>
</table>
| Efficacy of bisphosphonates for preventing hip fracture and reducing mortality | - Meta-analysis of four studies (n=3,088), elderly patients with hip fracture.  
- Comparison of patients on bisphosphonate and controls.  
- Bisphosphonate group had significantly lower mortality (34%).  
- Bisphosphonate group had significantly lower second hip fractures (40%).  
- No difference in overall complication rates between two groups. |
| **Zhou (2016b)**  | **Key points:**                                                         |
| Comparing efficacy of 7 bisphosphonates to reduce | - Meta-analysis of 36 studies, persons with primary osteoporosis.  
- Seven drugs significantly reduced chance of vertebral fracture, with zoledronic acid (ZA) |
<table>
<thead>
<tr>
<th>Citation</th>
<th>Content, Methods, Recommendations</th>
</tr>
</thead>
</table>
| fracture risk in primary osteoporosis | showing the greatest reduction.  
- Fracture risk in ZA 35% less than alendronate.  
- Fracture risk in ZA 47% less than clodronate.  
- Fracture risk in ZA 55% less than etidronate.  
- Fracture risk in ZA 48% less than ibandronate.  
- Fracture risk in ZA 41% less than risedronate.  
- Fracture risk in ZA 69% less than tiludronate. |
| Ma (2016) | Key points:  
- Meta-analysis of 34 studies (n=11,090).  
- Higher ibandronate efficacy predicted for patients with longer duration treatment (one to five years); increasing age; history of previous fractures; lower baseline T score; higher baseline levels of C-terminal telopeptide of type 1 collagen. |
| Chen (2015a) | Key points:  
- Meta-analysis of 13 studies (n=3,647) of men with osteoporosis.  
- BMD increase for each of eight drugs compared with placebo.  
- Used standardized mean differences (SMD) for each drug.  
- SMD for zoledronate = 13.48.  
- SMD for alendronate = 11.04.  
- SMD for teriparatide = 10.98.  
- SMD for risedronate = 10.33.  
- SMD for teriparatide = 9.33.  
- SMD for strontium ranelate = 8.88.  
- SMD for ibandronate = 5.49.  
- SMD for parathyroid hormone = 4.89.  
- SMD for alfacalcidol = 3.42. |

**References**

**Professional society guidelines/other:**


**Peer-reviewed references:**


**CMS National Coverage Determinations (NCDs):**

No NCDs identified as of the writing of this policy.

**Local Coverage Determinations:**


Zoledronic acid — Medicare has determined that providers can no longer bill J3487 (Zometa) and J3488 (Reclast) as of July 2013. Providers can bill Q2051 (Injection, Zoledronic Acid, Not Otherwise specified, and 1 mg). The LCD for this service is the following:

<table>
<thead>
<tr>
<th>LCD ID</th>
<th>LCD name</th>
<th>Contractor/state</th>
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</thead>
<tbody>
<tr>
<td>L30035</td>
<td>Drugs and Biologicals: Zoledronic Acid</td>
<td>Cahaba GBA/Georgia and Tennessee</td>
</tr>
<tr>
<td>L32110</td>
<td>Bisphosphonates (Intravenous [IV]) and Monoclonal Antibodies in the Treatment of Osteoporosis and Their Other Indications</td>
<td>First Coast Service Options/Florida (Part A)</td>
</tr>
<tr>
<td>L32100</td>
<td>Bisphosphonates (Intravenous [IV]) and Monoclonal Antibodies in the Treatment of Osteoporosis and Their Other Indications</td>
<td>First Coast Service Options/Florida (Part B)</td>
</tr>
</tbody>
</table>

Commonly submitted codes

Below are the most commonly submitted codes for the service(s)/item(s) subject to this policy. This is not an exhaustive list of codes. Providers are expected to consult the appropriate coding manuals and bill accordingly.

<table>
<thead>
<tr>
<th>CPT Code</th>
<th>Description</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>96374</td>
<td>Therapeutic, prophylactic or diagnostic injection (specify substance or drug); intravenous push, single or initial substance/drug (list separately in addition to code for primary procedure).</td>
<td></td>
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</tbody>
</table>

<table>
<thead>
<tr>
<th>ICD-10 Code</th>
<th>Description</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>M80.0</td>
<td>Age-related osteoporosis with pathological fracture without current pathological fracture</td>
<td>Requires a fifth digit to be valid</td>
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<tr>
<td>M80.81</td>
<td>Other osteoporosis with pathological fracture, shoulder</td>
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<tr>
<td>M80.841S</td>
<td>Other osteoporosis with current pathological fracture, right hand, sequela</td>
<td></td>
</tr>
<tr>
<td>M80.819S</td>
<td>Other osteoporosis with current pathological fracture, unspecified shoulder, sequela</td>
<td></td>
</tr>
<tr>
<td>ICD-10 Code</td>
<td>Description</td>
<td>Comments</td>
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<tr>
<td>M80.849A</td>
<td>Other osteoporosis with current pathological fracture, unspecified hand, initial encounter for fracture</td>
<td></td>
</tr>
<tr>
<td>M80.812S</td>
<td>Other osteoporosis with current pathological fracture, left shoulder, sequela</td>
<td></td>
</tr>
<tr>
<td>M80.811S</td>
<td>Other osteoporosis with current pathological fracture, right shoulder, sequela</td>
<td></td>
</tr>
<tr>
<td>M80.842A</td>
<td>Other osteoporosis with current pathological fracture, left hand, initial encounter for fracture</td>
<td></td>
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<tr>
<td>M80.841A</td>
<td>Other osteoporosis with current pathological fracture, right hand, initial encounter for fracture</td>
<td></td>
</tr>
<tr>
<td>M80.859S</td>
<td>Other osteoporosis with current pathological fracture, unspecified femur, sequela</td>
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<tr>
<td>M80.869S</td>
<td>Other osteoporosis with current pathological fracture, unspecified lower leg, sequela</td>
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<tr>
<td>M80.852S</td>
<td>Other osteoporosis with current pathological fracture, left femur, sequela</td>
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<tr>
<td>M80.862S</td>
<td>Other osteoporosis with current pathological fracture, left lower leg, sequela</td>
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<tr>
<td>M80.851S</td>
<td>Other osteoporosis with current pathological fracture, right femur, sequela</td>
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<td>M80.861S</td>
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<td>M80.80xS</td>
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</tr>
<tr>
<td>M80.819A</td>
<td>Other osteoporosis with current pathological fracture, unspecified shoulder, initial encounter for fracture</td>
<td>Requires a sixth and seventh digit to be valid</td>
</tr>
<tr>
<td>M81.0</td>
<td>Age-related osteoporosis without pathological fracture</td>
<td>Requires a fifth digit to be valid</td>
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<td>M81.6</td>
<td>Localized osteoporosis [Lequesne]</td>
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<tr>
<td>M81.8</td>
<td>Other osteoporosis without current pathological fracture</td>
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<tr>
<td>M80.0</td>
<td>Age-related osteoporosis with pathological fracture without current pathological fracture</td>
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</table>

<table>
<thead>
<tr>
<th>HCPCS Level II Code</th>
<th>Description</th>
<th>Comments</th>
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<tbody>
<tr>
<td>J0897</td>
<td>Subcutaneous, denosumab, 1 mg</td>
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<tr>
<td>J1740</td>
<td>Injection, ibandronate sodium, 1 mg</td>
<td></td>
</tr>
<tr>
<td>J3110</td>
<td>Subcutaneous, teriparatide, 10 mcg</td>
<td></td>
</tr>
<tr>
<td>J3489</td>
<td>IV, zoledronic acid, 1 mg</td>
<td></td>
</tr>
</tbody>
</table>

**Appendix 1**

PerformRx policy for agents for osteoporosis

<table>
<thead>
<tr>
<th>Field name</th>
<th>Field description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Prior Authorization Group Description</td>
<td>Injectable/Infusible Osteoporosis Agents</td>
</tr>
<tr>
<td>Drugs</td>
<td>Boniva® Injection (ibandronate), Forteo® (teriparatide), Prolia™ (denosumab), Reclast® (zoledronic acid) or any other newly marketed agent</td>
</tr>
<tr>
<td>Covered Uses</td>
<td>Medically accepted indications are defined using the following sources: the U.S. Food and Drug Administration (FDA), Micromedex, American Hospital Formulary Service (AHFS), United States Pharmacopeia Drug Information for the Healthcare Professional (USP DI), the Drug Package Insert (PPI), or disease state specific standard of care guidelines.</td>
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<td>Exclusion Criteria</td>
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<td>Field name</td>
<td>Field description</td>
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<tr>
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<td>----------------------------------------------------------------------------------------------------------------------------------------------------</td>
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<tr>
<td>Age Restrictions</td>
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<tr>
<td>Prescriber Restrictions</td>
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<tr>
<td>Coverage Duration</td>
<td>If all of the conditions are met, requests will be approved for a 1 year. <strong>FORTEO REQUESTS WILL ONLY BE APPROVED FOR A TOTAL DURATION OF 24 MONTHS.</strong> If the conditions are not met, the request will be sent to a Medical Director/clinical reviewer for medical necessity review.</td>
</tr>
</tbody>
</table>

**Other Criteria**

- If diagnosis is osteoporosis, documentation was submitted indicating patient is postmenopausal woman or a male patient with a bone mineral density (BMD) value consistent with osteoporosis (T-scores equal to or less than -2.5) or has had an osteoporotic fracture, OR patient is over age of 50 with a T-score between -1 and -2.5 at the femoral neck or spine and a 10-year hip fracture probability >3% or a 10-year major osteoporosis-related fracture probability >20%, based on the U.S.-adapted WHO absolute fracture risk model.
- The patient has a documented (consistent with pharmacy claims) adequate trial of an oral bisphosphonate or has a medical reason (e.g., intolerance, hypersensitivity, contraindication, etc.) for not using an oral bisphosphonate.
- If request is for **Forteo** (teriparatide) the patient has not exceeded a total of 24 months of therapy AND one of the following applies to patient:
  - Patient has documented trial and failure of Boniva (ibandronate) injection, Reclast (zoledronic acid), or Prolia (denosumab) or has a medical reason (e.g., intolerance, contraindication, etc.) why these therapies are not suitable to be used.
  - Has SEVERE osteoporosis (T-score -3.5 or below, or T-score of -2.5 or below plus a fragility fracture.

**Physician/clinical reviewer must override criteria when, in his/her professional judgment, the requested item is medically necessary.**

Revision/Review Date 8/2016