Name of Policy:  
Boniva® (Ibandronate Sodium) Infusion

Policy #: 266  
Category: Pharmacology  
Latest Review Date: April 2010  
Policy Grade: Active Policy but no longer scheduled for regular literature reviews and updates.

Background/Definitions:
As a general rule, benefits are payable under Blue Cross and Blue Shield of Alabama health plans only in cases of medical necessity and only if services or supplies are not investigational, provided the customer group contracts have such coverage.

The following Association Technology Evaluation Criteria must be met for a service/supply to be considered for coverage:

1. The technology must have final approval from the appropriate government regulatory bodies;
2. The scientific evidence must permit conclusions concerning the effect of the technology on health outcomes;
3. The technology must improve the net health outcome;
4. The technology must be as beneficial as any established alternatives;
5. The improvement must be attainable outside the investigational setting.

Medical Necessity means that health care services (e.g., procedures, treatments, supplies, devices, equipment, facilities or drugs) that a physician, exercising prudent clinical judgment, would provide to a patient for the purpose of preventing, evaluating, diagnosing or treating an illness, injury or disease or its symptoms, and that are:

1. In accordance with generally accepted standards of medical practice; and
2. Clinically appropriate in terms of type, frequency, extent, site and duration and considered effective for the patient’s illness, injury or disease; and
3. Not primarily for the convenience of the patient, physician or other health care provider; and
4. Not more costly than an alternative service or sequence of services at least as likely to produce equivalent therapeutic or diagnostic results as to the diagnosis or treatment of that patient’s illness, injury or disease.
Description of Procedure or Service:
Based on the World Health Organization Criteria, it is estimated that 15% of postmenopausal white women and 35% of women over 65 years of age in the U.S. have osteoporosis.

Boniva is a nitrogen-containing bisphosphonate that inhibits osteoclast-mediated bone resorption. Boniva Injection is intended for intravenous administration only.

Ibandronate inhibits osteoclast activity and reduces bone resorption and turnover. In postmenopausal women, it reduces the elevated rate of bone turnover, leading to, on average, a net gain in bone mass.

Boniva is available as an intravenous injection, given as 3 mg IV over 15-30 seconds, once every 3 months. All women in the studies received 400 IU Vitamin D and 500 mg calcium supplementation per day.

Boniva injection is indicated for the treatment of osteoporosis in post-menopausal women. It is contraindicated in patients with uncorrected hypocalcemia, or known hypersensitivity to Boniva. It may cause a transient decrease in serum calcium values. It must be administered intravenously and not by any other route. Patients who have Boniva injection should have serum creatinine measured prior to each dosage administration. It should not be administered to patients with severe renal impairment. It must be administered IV only by a health care professional.

Policy:
Effective for dates of service on or after June 19, 2009:
Boniva® (Ibandronate sodium) Injection, for intravenous administration, meets Blue Cross and Blue Shield of Alabama’s medical criteria for coverage when used for the following indications:

FDA Labeled Indications:
- Postmenopausal osteoporosis
- Postmenopausal osteoporosis; Prophylaxis

Non-FDA Labeled Indications:
- Bone metastasis from breast and prostate cancer
- Disorder related to renal transplantation-Osteoporosis
- Hypercalcemia of malignancy

Effective for dates of service on or after April 13, 2010:
Boniva® (Ibandronate sodium) Injection meets Blue Cross and Blue Shield of Alabama’s medical criteria for coverage for the treatment of men with osteoporosis.

Effective for dates of service prior to June 19, 2009:
Boniva® (Ibandronate sodium) Injection, for intravenous administration, meets Blue Cross and Blue Shield of Alabama’s medical criteria for coverage when used to treat osteoporosis in post-menopausal women with either of the following conditions:
• Documented inability to stand or sit upright for 60 minutes; **OR**
• Documented esophageal or gastric ulcer or esophageal stricture which would prohibit use of PO medications.

**Boniva® Injection**, for intravenous administration, **does not meet** Blue Cross and Blue Shield of Alabama’s medical criteria for coverage when used to treat other conditions, including, but not limited to:

- Pillburden
- Non-compliance

**Blue Cross and Blue Shield of Alabama does not approve or deny procedures, services, testing, or equipment for our members. Our decisions concern coverage only. The decision of whether or not to have a certain test, treatment or procedure is one made between the physician and his/her patient. Blue Cross and Blue Shield of Alabama administers benefits based on the members' contract and corporate medical policies. Physicians should always exercise their best medical judgment in providing the care they feel is most appropriate for their patients. Needed care should not be delayed or refused because of a coverage determination.**

**Key Points:**
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 humans, bone formation and resorption are closely linked; old bone is resorbed and replaced by newly formed bone. In post-menopausal osteoporosis, bone resorption exceeds bone formation, leading to bone loss and increased risk of fracture. After menopause, the risk of fractures of the spine and hip increases. Approximately 40% of 50 year old women will experience an osteoporosis-related fracture during their remaining lifetimes.

There are several studies published in peer-reviewed literature that evaluate the efficacy of IV ibandronate. Some of them are summarized below.

Stakkestad JA, et al (2003), reported on the efficacy, safety, and dose response of IV ibandronate given every 3 months. 629 post-menopausal women were randomly allocated to receive IV ibandronate, 0.5 mg, 1 mg, 2 mg, or placebo every 3 months. At 1 year, the highest BMD gains occurred in women receiving 2 mg ibandronate. The authors concluded that IV ibandronate every 3 months might be an alternative to oral bisphosphonate and hormonal therapy to prevent bone loss in postmenopausal women.

Adami S, et al (2004), reported on the IRIS study which looked at the dose-response relationship with IV ibandronate in 520 post-menopausal women. Patients were randomized to receive either 2 mg (n=261) or 1 mg (n=131) ibandronate or placebo (n=128) IV injections, given once every
3 months. At 1 year, ibandronate therapy produced substantial and dose dependent increases in lumbar spine and hip BMD, and decreases in biochemical markers of bone turnover. The authors noted that there are ongoing studies looking at the efficacy and convenience of intermittent IV ibandronate injections in post-menopausal osteoporosis.

The DIVA (Dosing Intravenous Administration) Study was presented at the 2005 annual meeting of the American College of Rheumatology and published in the package information for Boniva Injection, by Roche.

The DIVA Study was a multinational, randomized, double-blind, active control multicenter study of 1,358 women with post-menopausal osteoporosis, age 55-80 years. It compares the efficacy, safety, and tolerability of the 2.5 mg oral regimen with IV regimen: 3 mg IV every 3 months. All patients received 400 IU of Vitamin D and 500 mg of calcium supplementation daily throughout the trial. The primary endpoint was lumbar spine bone mineral density at one-year. The result at one-year showed that the average increase in lumbar spine BMD in patients treated with Boniva Injection was statistically superior to that in patients treated with the daily oral tablets (4.5% vs. 3.5% for 2 treatments, respectively, p < 0.001). The study also showed that patients treated with Boniva Injection had consistently higher BMD increases in the total hip and other skeletal sites (femoral neck and trochanter) than patients treated with oral daily Boniva. The two-year findings from the DIVA study were presented at the 2005 Annual Scientific Meeting of the American College of Rheumatology, November 2005. These results showed the BMD at the lumbar spine increased more in the IV dosing group than in the daily oral dosing group (6.3% vs. 4.8%). There were substantial increases in bone density at the hip which were greater in the IV group than in the oral daily regimen group (3.1% vs. 2.2%). There were also clinically relevant decreases in bone breakdown observed in all treatment groups.

In the one-year study comparing Boniva Injection and Boniva tablets, the overall safety and tolerability profiles of the two dosing regimens were similar. The most common adverse effects regardless of causality were arthralgia, back pain, influenza, hypertension, abdominal pain, and nasopharyngitis. In some patients, acute phase reaction-like events have been reported, usually only after the first injection. In most cases no specific treatment was required and symptoms subsided in 24-48 hours. Boniva Injection should not be administered to patients with severe renal impairment.

Other indications are covered based on the off-label indications published in a drug compendium.

**Key Words:**
Boniva®, Ibandronate sodium, post-menopausal osteoporosis

**Approved by Governing Bodies:**
Boniva® injectable (Ibandronate Sodium), intravenous, was approved by the FDA January 6, 2006 for the treatment of post-menopausal osteoporosis.
**Benefit Application:**
Coverage is subject to member’s specific benefits. Group specific policy will supersede this policy when applicable.

ITS: Home Policy provisions apply
FEP contracts: Special benefit consideration may apply. Refer to member’s benefit plan.
Pre-certification requirements: Not applicable

**Current Coding:**
CPT Codes:  
- J3490 Unlisted code (Description of Boniva (Ibandronate Sodium))
- J1740 Injection, Ibandronate Sodium, 1 mg

**Effective for dates of service on or after January 1, 2007:**

**References:**

**Policy History:**
Medical Policy Group, April 2006 (3)
Medical Policy Administration Committee, April 2006
Available for comment April 25-June 8, 2006
Medical Policy Group, March 2007 (3)
Medical Policy Administration Committee, April 2007
Available for comment April 12-May 26, 2007
Medical Policy Group, October 2008 (3)
Medical Policy Administration Committee, November 2008
Available for comment October 23-December 8, 2008
Medical Policy Group, June 2009 (3)
Medical Policy Administration Committee, July 2009
Available for comment July 1-August 14, 2009
Medical Policy Group, April 2010 (3)
Medical Policy Administration Committee, May 1010
Available for comment May 7-June 21, 2010

Medical Policy Group, September 2012 (3): Effective September 14, 2012 this policy is no longer scheduled for regular literature reviews and updates.

This medical policy is not an authorization, certification, explanation of benefits, or a contract. Eligibility and benefits are determined on a case-by-case basis according to the terms of the member’s plan in effect as of the date services are rendered. All medical policies are based on (i) research of current medical literature and (ii) review of common medical practices in the treatment and diagnosis of disease as of the date hereof. Physicians and other providers are solely responsible for all aspects of medical care and treatment, including the type, quality, and levels of care and treatment.

This policy is intended to be used for adjudication of claims (including pre-admission certification, pre-determinations, and pre-procedure review) in Blue Cross and Blue Shield’s administration of plan contracts.