ARCHIVED 8/22/18

BlueCross BlueShield of Alabama

Name of Blue Advantage Policy:
Boniva® (Ibandronate Sodium) Infusion

Policy #: 266
Category: Pharmacology

Latest Review Date: April 2010
Policy Grade: **Effective 9/14/2012: Active Policy but no longer scheduled for regular literature reviews and updates.**

Background:

Blue Advantage *medical policy does not conflict with Local Coverage Determinations (LCDs), Local Medical Review Policies (LMRPs) or National Coverage Determinations (NCDs) or with coverage provisions in Medicare manuals, instructions or operational policy letters. In order to be covered by Blue Advantage the service shall be reasonable and necessary under Title XVIII of the Social Security Act, Section 1862(a)(1)(A). The service is considered reasonable and necessary if it is determined that the service is:*

1. *Safe and effective;*
2. *Not experimental or investigational*;*
3. *Appropriate, including duration and frequency that is considered appropriate for the service, in terms of whether it is:*
   - *Furnished in accordance with accepted standards of medical practice for the diagnosis or treatment of the patient's condition or to improve the function of a malformed body member;*
   - *Furnished in a setting appropriate to the patient's medical needs and condition;*
   - *Ordered and furnished by qualified personnel;*
   - *One that meets, but does not exceed, the patient's medical need; and*
   - *At least as beneficial as an existing and available medically appropriate alternative.*

Routine costs of qualifying clinical trial services with dates of service on or after September 19, 2000 which meet the requirements of the Clinical Trials NCD are considered reasonable and necessary by Medicare. Providers should bill* ***Original Medicare* *for covered services that are related to* ***clinical trials*** *that meet Medicare requirements (Refer to Medicare National Coverage Determinations Manual, Chapter 1, Section 310 and Medicare Claims Processing Manual Chapter 32, Sections 69.0-69.11).*

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 3mg IV over 15 to 30 seconds, once every three 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 23, 2009:

Blue Advantage will treat **Boniva® (Ibandronate sodium) Injection**, for intravenous administration, as a **covered** benefit 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 27, 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 June 20, 2006 through June 22, 2009:

Blue Advantage will treat **Boniva® (Ibandronate sodium) Injection**, for intravenous administration, as a **covered** benefit 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.

Blue Advantage will treat **Boniva® Injection**, for intravenous administration**,** as a **non-covered** benefit when used to treat other conditions, including, but not limited to:

- Pill burden
- Non-compliance

Blue Advantage 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 Advantage administers benefits based on the members' contract and 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 three months. 629 post-menopausal women were randomly allocated to receive IV ibandronate, 0.5 mg, 1mg, 2mg, or placebo every three months. At 1year, the highest BMD gains occurred in women receiving 2mg ibandronate. The authors concluded that IV ibandronate every three 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 2mg (n=261) or 1mg (n=131) ibandronate or placebo (n=128) IV injections, given once every three months. At one 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 to 80 years. It compares the efficacy, safety, and tolerability of the 2.5 mg oral regimine with IV regimine: 3mg IV every three 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 two 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 regimine 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 to 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.

Current Coding:

CPT code:	**J1740**	Injection, Ibandronate Sodium, 1 mg **(Effective January 1, 2007)**
	J3490	Unlisted code (Description of Boniva (Ibandronate Sodium)

References:

1. Adami S, et al. Efficacy and safety of ibandronate given by intravenous injection once every 3 months. Bone, May 2004; 34(5): 881-889.
2. Boniva (ibandronate sodium) Injection. Prescribing information, Roche Laboratories, Inc. 2006.
3. Emkey R, et al. Two-year efficacy and tolerability of intermittent intravenous ibandronate injections in post-menopausal osteoporosis: the DIVA study. Abstract presented at the Annual Meeting of the American College of Rheumatology, November 12-17, 2005, San Diego, CA.
4. Orange Book Cumulative Supplement 2, 26th edition, February 2006. Approval drug products with therapeutic equivalence evaluations. www.fda.gov/cder/orange/obcs.pdf.
5. Reginster JY. Oral and intravenous ibandronate in the management of post-menopausal osteoporosis: A comprehensive review. Current Pharmaceutical Design, January 2005; 11(28): 3711-3728.
6. Stakkastad JA, et al. Intravenous ibandronate injections given every three months: A new treatment option to prevent bone loss in post-menopausal women. Annals of the Rheumatic Diseases, October 2003; 62(10): 969-975.
7. U.S. Department of Health and Human Services. Bone health and osteoporosis: A report of the surgeon general. Office of the Surgeon General, 2004.
8. Wilson SA, et al. Ibandronate (Boniva) for treatment and prevention of osteoporosis in post-menopausal women. American Family Physician, January 2006, Vol. 73, No. 2.

Policy History:

Adopted for Blue Advantage, March 2006
Available for comment May 5-June 19, 2006
Medical Policy Group, March 2007
Available for comment April 13-May 27, 2007
Medical Policy Group, October 2008
Available for comment October 23-December 8, 2008
Medical Policy Group, June 2009
Available for comment June 23-August 6, 2009
Medical Policy Group, April 2010
Available for comment May 7-June 21, 2010

Medical Policy Group, September 2012: **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.