Instruct patients to take supplemental calcium and vitamin D if dietary intake is inadequate.

Severe Bone, Joint, and/or Muscle Pain

• Renal Toxicity

1.1 Treatment of Postmenopausal Osteoporosis

2.1 Important Administration Instructions

BONIVA® (ibandronate sodium) Injection

• Hypocalcemia
• Hypersensitivity to BONIVA Injection

• Osteonecrosis of the Jaw (ONJ)
• Tissue Damage Related to Inappropriate Administration
• Osteonecrosis of the Jaw (ONJ)
• Tissue Damage Related to Inappropriate Administration
• Osteonecrosis of the Jaw (ONJ)
• Tissue Damage Related to Inappropriate Administration
• Osteonecrosis of the Jaw (ONJ)
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2.3 Laboratory Testing and Oral Examination Prior to Administration

1.1 Treatment of Postmenopausal Osteoporosis

2.1 Important Administration Instructions

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2.3 Laboratory Testing and Oral Examination Prior to Administration

1.1 Treatment of Postmenopausal Osteoporosis

2.1 Important Administration Instructions

BONIVA® (ibandronate sodium) Injection
BONIVA® (ibandronate sodium) Injection

be performed by the prescriber prior to initiation of bisphosphonate treatment. Consider a dental examination with appropriate preventive dentistry prior to treatment with bisphosphonates in patients with a history of concomitant risk factors (e.g., cancer, chemotherapy, radiotherapy, corticosteroids, poor oral hygiene, pre-existing dental disease or infection, anemia, coagulopathy).

While on treatment, patients with concomitant risk factors should avoid invasive dental procedures if possible. For patients who develop ONJ while on bisphosphonate therapy, dental surgery may exacerbate the condition. For patients requiring dental procedures, there are no data available to suggest whether discontinuation of bisphosphonate treatment reduces the risk of ONJ. The clinical judgment of the treating physician should guide the management plan of each patient based on individual benefit/risk assessment (see Adverse Reactions (6.4)).

5.6 Musculoskeletal Disorders

Severe and occasionally incapacitating bone, joint, and/or muscle pain has been reported in patients taking BONIVA and other bisphosphonates (see Adverse Reactions (6.2)).

The time to onset of symptoms varied from 1 day to several months after starting the drug. Most patients had relief of symptoms after stopping the bisphosphonate. A subset of patients had recurrence of symptoms when rechallenged with the same drug or another bisphosphonate. Discontinue BONIVA if severe symptoms develop.

5.7 Atypical Subtrochanteric and Diaphyseal Femoral Fractures

Atypical, low-energy, or low-trauma fractures of the femoral shaft have been reported in bisphosphonate-treated patients. These fractures can occur anywhere in the femoral shaft from just below the lesser trochanter to above the metaphysis and can be transverse or short oblique in orientation without evidence of comminution. Causality has not been established as these fractures also occur in osteoporotic patients who have not been treated with bisphosphonates. Atypical femur fractures most commonly occur with minimal or no trauma to the affected area. They may be bilateral and many patients report prodromal pain in the affected area, usually presenting as aching, dull thigh pain, weeks to months before a complete fracture occurs. A number of reports note that patients were also receiving treatment with glucocorticoids (e.g. prednisone) at the time of fracture. Any patient with a history of bisphosphonate exposure who presents with thigh or groin pain should be suspected of having an atypical fracture and should be evaluated to rule out an incomplete femur fracture. Patients presenting with an atypical fracture should also be assessed for symptoms and signs of fracture in the contralateral limb. Interruption of bisphosphonate therapy should be considered, pending a risk/benefit assessment, on an individual basis.

6 ADVERSE REACTIONS

Adverse reactions that appear in other sections of the labeling include:

- Hypocalcemia and Mineral Metabolism (see Warnings and Precautions (5.1))
- Anaphylactic Reaction (see Warnings and Precautions (5.2))
- Renal Impairment (see Warnings and Precautions (5.3))
- Tissue Damage Related to Inappropriate Drug Administration (see Warnings and Precautions (5.4))
- Osteonecrosis of the Jaw (see Warnings and Precautions (5.5))
- Musculoskeletal Pain (see Warnings and Precautions (5.6))
- Atypical Subtrochanteric and Diaphyseal Femoral Fractures (see Warnings and Precautions (5.7))

6.1 Clinical Trials Experience

Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a drug cannot be directly compared to rates in the clinical trials of another drug and may not reflect the rates observed in practice.

Quarterly Intravenous Injection

In a 1-year, double-blind, multicenter study comparing BONIVA Injection administered intravenously as 3 mg every 3 months to BONIVA 2.5 mg daily oral tablet in women with postmenopausal osteoporosis, the overall safety and tolerability profiles of the two dosing regimens were similar. The incidence of serious adverse reactions was 8.0% in the BONIVA 2.5 mg daily group and 7.5% in the BONIVA Injection 3 mg every 3 months group. The percentage of patients who withdrew from treatment due to adverse reactions was approximately 6.7% in the BONIVA 2.5 mg daily group and 8.5% in the BONIVA Injection 3 mg every 3 months group. Table 1 lists the adverse reactions reported in greater than 2% of patients.

<table>
<thead>
<tr>
<th>BONIVA® (ibandronate sodium) Injection</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Table 1 Adverse Reactions With an Incidence of at Least 2% in Patients Treated With BONIVA Injection (3 mg once every 3 months) or BONIVA Daily Oral Tablet (2.5 mg)</strong></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Body System/Adverse Reaction</th>
<th>BONIVA 2.5 mg Daily (Oral)</th>
<th>BONIVA 3 mg every 3 months (Intravenous)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Infections and Infestations</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Influenza</td>
<td>5</td>
<td>8</td>
</tr>
<tr>
<td>Nasopharyngitis</td>
<td>6</td>
<td>3</td>
</tr>
<tr>
<td>Pharyngitis</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>Gastroenteritis</td>
<td>3</td>
<td>3</td>
</tr>
<tr>
<td>Urinary Tract Infection</td>
<td>3</td>
<td>3</td>
</tr>
<tr>
<td>Bronchitis</td>
<td>3</td>
<td>3</td>
</tr>
<tr>
<td>Upper Respiratory Tract Infection</td>
<td>4</td>
<td>3</td>
</tr>
<tr>
<td><strong>Gastrointestinal Disorders</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Abdominal Pain*</td>
<td>6</td>
<td>5</td>
</tr>
<tr>
<td>Dyspepsia</td>
<td>4</td>
<td>4</td>
</tr>
<tr>
<td>Nausea</td>
<td>4</td>
<td>2</td>
</tr>
<tr>
<td>Constipation</td>
<td>4</td>
<td>3</td>
</tr>
<tr>
<td>Diarrhea</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>Gastritis</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td><strong>Musculoskeletal and Connective Tissue Disorders</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Arthralgia</td>
<td>9</td>
<td>10</td>
</tr>
<tr>
<td>Back Pain</td>
<td>8</td>
<td>8</td>
</tr>
<tr>
<td>Localized Osteoarthritides</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>Pain in Extremity</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>Myalgia</td>
<td>1</td>
<td>3</td>
</tr>
<tr>
<td><strong>Nervous System Disorders</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Dizziness</td>
<td>3</td>
<td>2</td>
</tr>
<tr>
<td>Headache</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td><strong>Psychiatric Disorders</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Insomnia</td>
<td>3</td>
<td>1</td>
</tr>
<tr>
<td>Depression</td>
<td>5</td>
<td>5</td>
</tr>
<tr>
<td><strong>General Disorders and Administration Site Conditions</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Influenza-like Illness†</td>
<td>1</td>
<td>5</td>
</tr>
<tr>
<td>Fatigue</td>
<td>4</td>
<td>3</td>
</tr>
<tr>
<td><strong>Skin and Subcutaneous Tissue Disorders</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Rash</td>
<td>3</td>
<td>3</td>
</tr>
<tr>
<td><strong>Acute Phase Reaction-like Events</strong></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

†Combination of abdominal pain and abdominal pain upper.

‡Combination of influenza-like illness and acute phase reaction.

−Combination of rash, pruritic rash, macular rash, dermatitis, dermatitis allergic, exanthema, erythema, rash papular, rash generalized, dermatitis medicamentos, rash erythematous

Gastrointestinal Adverse Reactions

The incidence of selected gastrointestinal adverse reactions in the placebo and BONIVA 2.5 mg daily groups was: dyspepsia (10% vs. 12%), diarrhea (5% vs. 7%), and abdominal pain (5% vs. 6%).

Musculoskeletal Adverse Reactions

The incidence of selected musculoskeletal adverse reactions in the placebo and BONIVA 2.5 mg daily groups were: back pain (12% vs. 14%), arthralgia (14% vs. 14%) and myalgia (5% vs. 6%).

6.2 Postmarketing Experience

The following adverse reactions have been identified during post-approval use of BONIVA Injection. Because these reactions are reported voluntarily from a population of uncertain size, it is not always possible to reliably estimate their frequency or establish a causal relationship to drug exposure.

Hypersensitivity: Allergic reactions including anaphylaxis with fatalities, angioedema, asthma exacerbation, bronchoconstriction, and rash (see Contraindications (4), Warnings and Precautions (5.2)).

Hypocalcemia: Hypocalcemia (see Warnings and Precautions (5.1)).

Musculoskeletal Pain: Bone, joint, or muscle pain (musculoskeletal pain), described as severe or incapacitating (see Warnings and Precautions (5.2)).

Osteonecrosis of the Jaw: Osteonecrosis of the jaw (see Warnings and Precautions (5.5)).

Musculoskeletal Pain: Bone, joint, or muscle pain (musculoskeletal pain), described as severe or incapacitating (see Warnings and Precautions (5.2)).

Atypical Femoral Shaft Fracture: Atypical, low-energy, or low-trauma fracture of the femoral shaft (see Warnings and Precautions (5.7)).

Eye Inflammation: Irritis and uveitis. In some cases with other bisphosphonates, these events did not resolve until the bisphosphonate was discontinued.

7 DRUG INTERACTIONS

7.1 Mefloquine/Primaquine

Intravenous ibandronate (6 mg) did not interact with intravenous melphalan (10 mg/m²) or oral prednisolone (60 mg/m²). (See Clinical Pharmacology (12.3)).
with BONIVA Injection. Overdosage with intravenous bis-

10 OVERDOSAGE

WITH SEVERE RENAL IMPAIRMENT (CREATININE CLEARANCE LESS

8.6 Renal Impairment

The pharmacokinetics of ibandronate have not been studied in patients less than 18 years of age.

Geriatric

The pharmacokinetics of ibandronate are similar in both men and women.

Drug Interaction

Melphalan/Prednisolone

A pharmacokinetic interaction study in multiple myeloma patients demonstrated that intravenous melphalan (10 mg/m²) and prednisolone (60 mg/m²) did not interact with 6 mg ibandronate upon intravenous coadministration. Ibandronate did not interact with melphalan or prednisolone.

Tamoxifen

A pharmacokinetic interaction study in healthy postmeno-
pausal women demonstrated that there was no interaction between oral 30 mg tamoxifen and intravenous 2 mg ibandronate.

13 NONCLINICAL TOXICOLONY

13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility

Carcinogenesis

In a 104-week carcinogenicity study, doses of 3, 7, or 15 mg/kg/day were administered by oral gavage to Wistar rats (systemic exposures in males and females up to 3 and 1 times, respectively, human exposure). There were no significant drug-related tumor findings in male or female rats. In a 78-week carcinogenicity study, doses of 5, 20, or 40 mg/kg/day were administered by oral gavage to NMRI mice (exposures in males and females up to 96 and 14 times, respectively, human exposure). There were no significant drug-related tumor findings in male or female mice. In a 50-week carcinogenicity study, doses of 10 mg/kg/day were administered in the drinking water to NMRI mice. A dose-related increased incidence of adrenal subcapsular adenoma/carcinoma was observed in female mice, which was sta-
tistically significant at 80 mg/kg/day (32 to 51 times human exposure). The relevance of these findings to humans is unknown.
**BONIVA® (ibandronate sodium) Injection**

Exposure multiples comparing human and rodent doses were calculated using human exposure at the recommended intravenous dose of 3 mg every 3 months, based on cumulative AUC comparison.

**Mutagenesis**

There was no evidence for a mutagenic or clastogenic potential of ibandronate in the following assays: in vitro bacterial mutagenesis assay in Salmonella typhimurium and Escherichia coli, individual cell-based mutagenesis assay in Chinese hamster V79 cells, and chromosomal aberration test in human peripheral lymphocytes, each with and without metabolic activation. Ibandronate was not genotoxic in the in vivo mouse micronucleus tests for chromosomal damage.

**Rat Pregnancy and Fertility**

In female rats treated from 14 days prior to mating through gestation, decreases in fertility, corpora lutea and implantation sites, and increased preimplantation loss were observed at an intravenous dose of 1.2 mg/kg/day (317 times human exposure). In male rats treated for 28 days prior to mating, a decrease in sperm production and altered sperm morphology were observed at intravenous doses greater than or equal to 0.3 mg/kg/day (greater than or equal to 40 times human exposure).

Exposure multiples comparing human and rat doses were calculated using human exposure at the recommended intravenous dose of 3 mg every 3 months, based on cumulative AUC comparison.

### 13.2 Animal Pharmacology

**Animals**

Studies have shown that ibandronate is an inhibitor of osteoclast-mediated bone resorption. In the Schenk assay in growing rats, ibandronate inhibited bone resorption and increased bone volume, based on histologic examination of the tibial metaphyses. There was no evidence of impaired mineralization at the highest dose of 5 mg/kg/day (excutaneous), with doses 500 times lower than the highest intravenous dose of 0.005 mg/kg/day in this model, and 5000 times the optimal antiresorptive dose of 0.001 mg/kg/day in the aged osteoclastoma. Ibandronate indicates that BONIVA Injection administered at a therapeutic dose is unlikely to induce osteomalacia.

**Long-term**

Daily or intermittent administration of ibandronate to ovariectomized rats or monkeys was associated with suppression of bone turnover and increases in bone mass. Vertebral BMD, trabecular density, and biomechanical strength of bone were demonstrated in a randomized, double-blind, placebo-controlled, multinational study (Treatment Study) of 2946 women aged 55 to 80 years, who were on average 21 years postmenopause, who had a lumbar spine BMD 2 to 5 SD below the premenopausal mean (T-score) in at least one vertebra (L1-L4), and who had one to four prevalent vertebral fractures. BONIVA was evaluated in oral doses of 2.5 mg daily and 20 mg intermittently. The main outcome measure was the occurrence of new radiographically diagnosed, vertebral fractures after 3 years of treatment. The diagnosis of an incident vertebral fracture was based on both qualitative diagnosis by the radiologist and quantitative morphometric criteria. The morphometric diagnosis required the dual occurrence of two events: a relative height ratio or relative height reduction in a vertebral body of at least 20%, together with at least a 4 mm absolute decrease in height. All women received 400 international units vitamin D and 500 mg calcium supplementation per day.

**Effect on Vertebral Fracture**

BONIVA 2.5 mg daily oral tablet significantly reduced the incidence of new vertebral fractures compared to placebo. Over the course of the 3-year study, the risk for new vertebral fracture was 9.6% in the placebo-treated women and 4.7% in the women treated with BONIVA 2.5 mg daily oral tablet (p<0.001) (see Table 3). [See table 3 below]

### Table 3 Effect of BONIVA Daily Oral Tablet on the Incidence of Vertebral Fracture in the 3-Year Osteoporosis Treatment Study**

<table>
<thead>
<tr>
<th>Proportion of Patients with Fracture (%)</th>
<th>Placebo</th>
<th>BONIVA 2.5 mg Daily Oral Tablet or Placebo in the 3-Year Osteoporosis Treatment Study*</th>
</tr>
</thead>
<tbody>
<tr>
<td>New Vertebral Fracture</td>
<td>9.6</td>
<td>4.7</td>
</tr>
<tr>
<td>0-3 Year</td>
<td></td>
<td>4.9</td>
</tr>
<tr>
<td></td>
<td></td>
<td>(2.3, 7.4)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>(25, 68)</td>
</tr>
<tr>
<td>New and Worsening Vertebral Fracture</td>
<td>10.4</td>
<td>5.1</td>
</tr>
<tr>
<td>0-3 Year</td>
<td></td>
<td>5.3</td>
</tr>
<tr>
<td></td>
<td></td>
<td>(2.6, 7.9)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>(30, 67)</td>
</tr>
<tr>
<td>Clinical (Symptomatic) Vertebral Fracture</td>
<td>5.3</td>
<td>2.8</td>
</tr>
<tr>
<td>0-3 Year</td>
<td></td>
<td>2.5</td>
</tr>
<tr>
<td></td>
<td></td>
<td>(0.6, 4.5)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>(14, 69)</td>
</tr>
</tbody>
</table>

**The endpoint value is the value at the study’s last time point, 3 years, for all patients who had BMD measured at that time, otherwise the last postbaseline value prior to the study’s last time point is used.

**BONIVA® (ibandronate sodium) Injection**

**Exposure**

In the in vitro-to-treat (ITT) efficacy analysis, the least-squares mean increase at 1 year in lumbar spine BMD in patients (n=429) treated with BONIVA Injection 3 mg once every 3 months (4.5%) was statistically superior to that in patients (n=434) treated with daily oral tablets (3.4%). The mean difference between groups was 1.1% (95% confidence interval: 0.5%, 1.6%; p<0.001; see Figure 1). The mean increase from baseline in total hip BMD at 1 year was 2.1% in the BONIVA Injection 3 mg once every 3 months group and 1.5% in the BONIVA 2.5 mg daily oral tablet group. Consistent higher BMD increases at the femoral neck and trochanter were also observed following BONIVA Injection once every 3 months compared to BONIVA 2.5 mg daily oral tablet.

### Table 4 Mean Percent Change in BMD from Baseline to Endpoint in Patients Treated with BONIVA 2.5 mg Daily Oral Tablet or Placebo in the 3-Year Osteoporosis Treatment Study*

<table>
<thead>
<tr>
<th>BONIVA 2.5 mg Daily Oral Tablet</th>
<th>Placebo</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lumbar Spine</td>
<td>1.4</td>
</tr>
<tr>
<td>0-3 Year</td>
<td>(n=693)</td>
</tr>
<tr>
<td>Total Hip</td>
<td>0.7</td>
</tr>
<tr>
<td>0-3 Year</td>
<td>(n=658)</td>
</tr>
<tr>
<td>Femoral Neck</td>
<td>0.2</td>
</tr>
<tr>
<td>0-3 Year</td>
<td>(n=685)</td>
</tr>
<tr>
<td>Trochanter</td>
<td>0.3</td>
</tr>
<tr>
<td>0-3 Year</td>
<td>(n=699)</td>
</tr>
</tbody>
</table>

**The endpoint value is the value at the study’s last time point, 3 years, for all patients who had BMD measured at that time, otherwise the last postbaseline value prior to the study’s last time point is used.**

**Bone Histology**

The effects of BONIVA 2.5 mg daily oral tablet on bone histology were evaluated in iliac crest biopsies from 16 women after 22 months of treatment and 20 women after 34 months of treatment. The histological analyses of bone biopsies showed bone of normal quality and no indication of os- teomalacia or a mineralization defect.

### 16 HOW SUPPLIED/STORAGE AND HANDLING

**16.1 How Supplied**

**BONIVA Injection (ibandronate sodium) is supplied as a kit containing a 3 mg/3 mL single-use, clear glass, 5 mL (5 cc) prefilled syringe, a 25-gauge, 3/4 inch needle with wings, needle-stick protection device, and a 9 cm plastic tubing for attachment (NDC 0043 00 9985).**

**16.2 Storage and Handling**

Store at 25°C (77°F); excursions permitted between 15° and 30° C (59° and 86°F); see USP Controlled Room Temperature.

### 17 PATIENT COUNSELING INFORMATION

**“See FDA-approved patient labeling (Medication Guide)”**

Inform patients that BONIVA Injection must be administered intravenously by a health care professional. Patients should be instructed to read the Medication Guide carefully before BONIVA is administered and to re-read it each time the prescription is renewed because it contains important information the patient should know about BONIVA.

Inform patients that BONIVA Injection is administered once every 3 months. If the injection is missed, the injection should be administered as soon as it can be rescheduled. Thereafter, injections should be scheduled every 3 months from the date of the last injection. Do not administer BONIVA Injection more frequently than once every 3 months.

Inform patients that they should take supplemental calcium and vitamin D if their dietary intake is inadequate (see Warnings and Precautions (5.1)).

Inform patients BONIVA injection should not be administered to patients with creatinine clearance less than 30 mL/ min. A serum creatinine should be measured prior to each dose (see Warnings and Precautions (5.3)).

Inform patients that the most common side effects of BONIVA include arthralgia, back pain, hypertension, and abdominal pain. Flu-like symptoms (acute phase reaction) may occur within 3 days following infusion, and usually subside within 24-48 hours without specific therapy.
BONIVA® (ibandronate sodium) Injection

Inform patients that there have been reports of persistent pain and/or unusual bone fractures occurring near the mouth or jaw, primarily in patients treated with bisphosphonates for other illnesses. If they experience these symptoms, they should inform their physician or dentist.

Inform patients that severe bone, joint, and/or muscle pain have been reported in patients taking bisphosphonates, including BONIVA. Patients should report severe symptoms if they develop.

Inform patients that atypical femur fractures in patients on bisphosphonate therapy have been reported. Patients should report new thigh or groin pain and undergo evaluation to rule out a femoral fracture.

MEDICATION GUIDE

BONIVA® (Bon-EE-va) Injection for intravenous use

Read the Medication Guide that comes with BONIVA before you start taking it and each time you get a refill. There may be new information. This Medication Guide does not take the place of talking with your doctor about your medical condition or treatment. Talk to your doctor if you have any questions about BONIVA.

What is the most important information I should know about BONIVA?

BONIVA Injection is given in your vein (intravenously) and only given by a healthcare provider. Do not give BONIVA Injection to yourself.

BONIVA may cause serious side effects including:
1. Low calcium levels in your blood (hypocalcemia)
2. Severe allergic reactions (anaphylactic reaction)
3. Severe kidney problems
4. Severe jaw bone problems (osteonecrosis)
5. Bone, joint or muscle pain
6. Unusual thigh bone fractures

UMC 20612

Low calcium levels in your blood (hypocalcemia)

BONIVA may lower the calcium levels in your blood. If you have low blood calcium before you start taking BONIVA, it may get worse during treatment. Your low blood calcium must be treated before you receive BONIVA. Most people with low blood calcium levels do not have symptoms, but some people may have symptoms. Call your doctor right away if you have symptoms of low blood calcium such as:
- Spasms, twitches, or cramps in your muscles
- Numbness or tingling in your fingers, toes, or around your mouth
- Trouble swallowing
- All of your teeth falling out
- Poor ability to swallow
- Unusual bleeding or bruising
- Weakness and muscle cramps
- Not being able to breathe
- Flulike symptoms
- Fever
- Chills
- Bone, joint, or muscle pain
- Fatigue

If you have flu-like symptoms, they should get better within 24 to 48 hours. Some people have pain or a sore that will not heal in their mouth or jaw while they receive BONIVA. Tell your doctor or dentist if you have mouth or jaw problems. Tell your doctor if you have any side effect that bothers you or that does not go away. These are not all the possible side effects of BONIVA. For more information, ask your doctor or pharmacist.

Call your doctor for medical advice about side effects. You may report side effects to FDA at 1-800-FDA-1088.

BONIVA® (ibandronate sodium) Injection

5. Bone, joint, or muscle pain:

Some people who receive BONIVA develop severe bone, joint, or muscle pain.

6. Unusual thigh bone fractures:

Some people have developed unusual fractures in their thigh bone. Symptoms of a fracture may include new or unusual pain in your hip, groin, or thigh.

Call your doctor right away if you have any of these side effects.

What is BONIVA?

BONIVA is a prescription medicine used to treat osteoporosis in women after menopause. BONIVA helps increase bone mass and helps reduce the chance of having a spinal fracture (break).

It is not known how long BONIVA works for the treatment of osteoporosis. You should see your doctor regularly to determine if BONIVA is still right for you. It is not known if BONIVA is safe and effective in children.

Who should not receive BONIVA?

Do not receive BONIVA if you:
- Have low levels of calcium in your blood
- Are allergic to ibandronate sodium or any of the ingredients in BONIVA

See the end of this leaflet for a complete list of ingredients in BONIVA.

What should I tell my healthcare provider before receiving BONIVA?

Before you receive BONIVA, tell your doctor if you:
- Have low blood calcium
- Plan to have dental surgery or teeth removed
- Have kidney problems or other problems that may affect your kidneys
- Have been told you have trouble absorbing minerals in your stomach or intestines (malabsorption syndrome)
- Are pregnant or plan to become pregnant. It is not known if BONIVA can harm your unborn baby.

Are breastfeeding or plan to breast-feed. It is not known if BONIVA passes into your milk and may harm your baby.

Tell your doctor and dentist about all the medicines you take, including prescription and non-prescription medicines, vitamins and herbal supplements.

Know the medicines you take. Keep a list of them and show it to your healthcare provider and pharmacist each time you get a new medicine.

How should I receive BONIVA?

BONIVA Injection is given 1 time every 3 months by a healthcare provider.

If you receive a dose of BONIVA, call your doctor or healthcare provider to schedule your next dose.

What are the possible side effects of BONIVA?

BONIVA may cause severe side effects. See "What is the most important information I should know about BONIVA?"

The most common side effects of BONIVA include:
- Pain in your bones, joints or muscles
- Back pain
- Abdominal pain

Flu-like symptoms may happen within 3 days after you receive BONIVA. Symptoms include:
- Fever
- Chills
- Bone, joint, or muscle pain
- Fatigue

If you have flu-like symptoms, they should get better within 24 to 48 hours. Some people have pain or a sore that will not heal in their mouth or jaw while they receive BONIVA. Tell your doctor or dentist if you have mouth or jaw problems.

Tell your doctor if you have any side effect that bothers you or that does not go away. These are not all the possible side effects of BONIVA. For more information, ask your doctor or pharmacist.

Call your doctor for medical advice about side effects. You may report side effects to FDA at 1-800-FDA-1088.

BONDIA® (ibandronate sodium) Injection

How should I store BONIVA if I need to pick it up from a pharmacy?

Store BONIVA Injection at room temperature between 68°F and 77°F (20°C and 25°C).

Keep BONIVA Injection and all medicines out of the reach of children.

General information about the safe and effective use of BONIVA.

Medicines are sometimes prescribed for purposes other than those listed in a Medication Guide. Do not use BONIVA for a condition for which it was not prescribed. Do not give BONIVA to other people, even if they have the same symptoms you have. It may harm them.

This Medication Guide summarizes the most important information about BONIVA. If you would like more information, talk with your doctor. You can ask your doctor or pharmacist for information about BONIVA that is written for health professionals.

What are the ingredients in BONIVA?

Active ingredient: ibandronate sodium Inactive ingredients: sodium chloride, glacial acetic acid, sodium acetate and water

This Medication Guide has been approved by the U.S. Food and Drug Administration.

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TERUMO® Surshield™ Safety Winged Infusion Set – Instructions for Use: IV Administration

Aseptic technique, proper skin preparation and continued protection of the site are essential. Observe Universal Precautions on all patients.

Caution: Keep hands behind the needle at all times during use and discard.

Instructions for Device Assembly

1. Open the package.
2. Remove the rubber cap from the tip of the syringe containing the BONIVA Injection and the protective SV cap from hub at the end of the tubing opposite the butterfly needle.
3. Insert the tip of the syringe into the hub and twist as firm pressure is applied to assure a tight connection.
4. Proceed with priming and confirm that administration fluid comes from the needle.

Venipuncture and Administration

1. Flip the safety shield back away from the needle towards the tubing. Grasp wings securely.
2. Remove the needle protector. Caution: Care should be taken not to touch the needle.
3. Perform venipuncture and confirm proper positioning of the needle in the vein.
4. Carefully allow wings to return to starting position and conform to the shape of the skin.
5. Further secure the position of the winged infusion set per facility protocol.

After Use

1. Remove tape, if present, from wings.
2. Flip the safety shield forward toward the needle. Grasp a wing and the safety shield between your thumb and index finger. Completely remove the needle from the puncture site and apply digital pressure to the site using a sterile gauze pad held in the opposite hand (Fig. 1).
3. With the wing and shield between your thumb and index finger pinch together (or press the safety shield against a hard surface such as a bedside table) until an audible click is heard (Fig. 2).
4. Visually confirm activation of the safety feature (Fig. 3).
5. Dispose of used needles and materials following the policies and procedures of your facility, as well as federal and local regulations for "Sharps Disposal."