Genentech
A Member of the Roche Group

IMPORTANT DRUG WARNING

June 2013

Subject: Important Change in the BONIVA® (ibandronate sodium) Injection Prescribing Information – Warning and Precaution Regarding Anaphylaxis (anaphylactic reaction, anaphylactic shock) Including Fatal Events

Dear Healthcare Professional,

BONIVA (ibandronate sodium) Injection is a nitrogen-containing bisphosphonate that is indicated for the treatment of osteoporosis in postmenopausal women. Genentech would like to inform you of important safety information concerning anaphylaxis that has been added to the Contraindications, Warnings and Precautions, and Adverse Reactions Sections of the BONIVA Injection Prescribing Information.

These important safety additions to the BONIVA Injection Prescribing Information are:

CONTRAINDICATIONS
Known hypersensitivity to BONIVA Injection or to any of its excipients. *Cases of anaphylaxis, including fatal events, have been reported.*

WARNINGS AND PRECAUTIONS
Cases of anaphylaxis, including fatal events, have been reported in patients treated with BONIVA Injection.

Appropriate medical support and monitoring measures should be readily available when BONIVA Injection is administered. If anaphylactic or other severe hypersensitivity/allergic reactions occur, immediately discontinue the injection and initiate appropriate treatment.

ADVERSE REACTIONS – Postmarketing Experience
Hypersensitivity: Allergic reactions including anaphylaxis with fatalities

The current Adverse Reactions – Postmarketing Experience Section of the BONIVA Tablets Prescribing Information includes allergic reactions, angioedema, bronchospasm and rash but is also being revised to include specific reference to anaphylactic reaction/shock, in some cases fatal.

Further information on the safety concern
Anaphylactic reaction/shock has been reported very rarely and within the background incidence in the postmenopausal osteoporosis population. There are no published reports on BONIVA and anaphylactic reaction/shock. However, in some cases reported to Roche/Genentech the clinical manifestations of anaphylaxis, including fatal outcomes, were present and the role of BONIVA could not be fully excluded.

Summary of Important Information about BONIVA (ibandronate sodium) Injection and Tablets

Indications
BONIVA Injection is indicated for the treatment of osteoporosis in postmenopausal women. BONIVA Tablets are indicated for the treatment and prevention of osteoporosis in postmenopausal women. In postmenopausal women with osteoporosis, BONIVA increases bone mineral density (BMD) and reduces the incidence of vertebral fractures.

The safety and effectiveness of BONIVA Injection for the treatment of osteoporosis are based on clinical data of one year duration. The optimal duration of use has not been determined. All patients on bisphosphonate therapy should have the need for continued therapy re-evaluated on a periodic basis. Patients at low-risk for fracture should be considered for drug discontinuation after 3 to 5 years of use. Patients who discontinue therapy should have their risk for fracture re-evaluated periodically.

The optimal duration of use for BONIVA Tablets has not been determined. The safety and effectiveness of BONIVA for the treatment of osteoporosis are based on clinical data of three years duration. All patients on bisphosphonate therapy should have the need for continued therapy re-evaluated on a periodic basis. Patients at low-risk for fracture should be considered for drug discontinuation after 3 to 5 years of use. Patients who discontinue therapy should have their risk for fracture re-evaluated periodically.

BONIVA **Injection** is contraindicated in patients with known hypersensivity to BONIVA Injection or to any of its excipients or uncorrected hypocalcemia. Hypocalcemia may worsen during treatment. Correct hypocalcemia before use. Cases of anaphylaxis, including fatal events, have been reported in patients treated with BONIVA Injection. Appropriate medical support and monitoring measures should be readily available when BONIVA Injection is administered. If anaphylactic or other severe hypersensitivity/allergic reactions occur, immediately discontinue the injection and initiate appropriate treatment.

Treatment with intravenous bisphosphonates has been associated with renal toxicity and acute renal failure. Do not administer Boniva Injection to patients with severe renal impairment (creatinine clearance less than 30 mL/min). Boniva Injection should be withheld in patients with renal deterioration.

BONIVA Injection must only be administered intravenously. Do not administer BONIVA Injection by any other route of administration.

Osteonecrosis of the jaw (ONJ) has been reported in patients treated with bisphosphonates, including BONIVA Injection. A routine oral examination should be performed by the prescriber prior to initiation of bisphosphonate treatment. While on treatment, patients with concomitant risk factors should avoid invasive dental procedures if possible. For patients requiring dental procedures, there are no data available to suggest whether discontinuation of bisphosphonate treatment reduces the risk of ONJ.

Severe and occasionally incapacitating bone, joint, and/or muscle pain has been reported in patients taking BONIVA and other bisphosphonates. Discontinue BONIVA if severe symptoms develop.

Atypical femur fractures have been reported. Patients with new thigh or groin pain should be evaluated to rule out an incomplete femoral fracture.

The most common adverse reactions (≥5%) of BONIVA Injection were arthralgia, back pain, hypertension, abdominal pain, influenza, and nasopharyngitis. In some patients, acute phase reaction-like events (10% BONIVA Injection vs 4% BONIVA Tablets) have been reported within 3 days of an IV dose and lasting for 7 days or less, most commonly after the first injection.

BONIVA **Tablets** are contraindicated in patients with abnormalities of the esophagus which delay esophageal emptying, the inability to stand or sit upright for at least 60 minutes, hypocalcemia, or known hypersensitivity to any component of this product. Cases of anaphylaxis have been reported.

Severe irritation of the upper gastrointestinal (GI) mucosa can occur. Dosing instructions should be followed and caution should be used in patients with active upper GI disease. Patients should discontinue use if new or worsening symptoms occur.

Hypocalcemia may worsen during treatment. Correct hypocalcemia before use.

Severe bone, joint, and muscle pain may occur. Consider discontinuing treatment if symptoms develop.

Osteonecrosis of the jaw (ONJ), which can occur spontaneously, is generally associated with tooth extraction and/or local infection with delayed healing, and has been reported in patients taking bisphosphonates, including BONIVA. The risk of ONJ may increase with duration of exposure to bisphosphonates. Discontinuation of bisphosphonate therapy should be considered based on individual benefit/risk assessment.

Atypical femur fractures have been reported. Patients with new thigh or groin pain should be evaluated to rule out an incomplete femoral fracture.

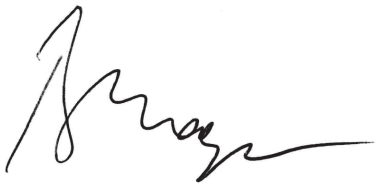
The most common adverse reactions (≥5%) of BONIVA 150 mg once-monthly Tablets are abdominal pain, hypertension, dyspepsia, arthralgia, nausea, and diarrhea.

Patients should be given and instructed to read the accompanying Medication Guide before starting treatment and at every injection or refill.

Please see the BONIVA Full Prescribing Information enclosed with this letter or visit www.gene.com for additional important safety information. If you have any questions or require additional information regarding the use of BONIVA, please contact our Medical Communications Group at 1-800-821-8590 from 5:30 AM to 4:00 PM Pacific Time, Monday through Friday.

As always, healthcare professionals are encouraged to report side effects associated with the use of BONIVA to Genentech at 1-888-835-2555. Alternatively, such information may be reported to FDA's MedWatch Safety Information and Adverse Event Reporting Program, either online at **www.fda.gov/medwatch**, by telephone (1-800-FDA-1088), by facsimile (1-800-FDA-0178), or by mail using the MedWatch Form FDA 3500 (FDA Medical Products Reporting Program, 5600 Fishers Lane, Rockville MD 20852-9787).

Sincerely,



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