

ספטמבר 2024

## Terrosa<sup>®</sup>, solution for injection

צוות רפואי נכבד,

חברת דקסל בע"מ מבקשת להודיעכם על עדכון והחמרה בעלון לרופא ובעלון לצרכן של התכשיר טרוזה.

בהודעה זו מפורטים העדכונים המהווים החמרה בלבד. למידע מלא, יש לעיין בעלונים.

העלונים לרופא ולצרכן נשלחו לפרסום במאגר התרופות שבאתר משרד הבריאות וניתן לקבלם מודפסים ע"י פנייה לבעל הרישום: דקסל בע"מ, רח' דקסל 1, אור עקיבא 3060000, ישראל, טל': 04-6364000.

### הרכב התכשיר:

Each cartridge contains: Teriparatide 250mcg/ml

### התוויות מאושרות:

**Treatment of postmenopausal women with osteoporosis at high risk for fracture:** Terrosa is indicated for the treatment of postmenopausal women with osteoporosis at high risk for fracture, defined as a history of osteoporotic fracture, multiple risk factors for fracture, or patients who have failed or are intolerant to other available osteoporosis therapy. In postmenopausal women with osteoporosis, Terrosa increases BMD, reduces the risk of vertebral and non-vertebral fractures

**Increase of bone mass in men with primary or hypogonadal osteoporosis at high risk for fracture:** Terrosa is indicated to increase bone mass in men with primary or hypogonadal osteoporosis at high risk for fracture, defined as a history of osteoporotic fracture, multiple risk factors for fracture, or patients who have failed or are intolerant to other available osteoporosis therapy.

**Treatment of men and women with glucocorticoid-induced osteoporosis at high risk for fracture:** Terrosa is indicated for the treatment of men and women with osteoporosis associated with sustained systemic glucocorticoid therapy (daily dosage equivalent to 5 mg or greater of prednisone) at high risk for fracture, defined as a history of osteoporotic fracture, multiple risk factors for fracture, or patients who have failed or are intolerant to other available osteoporosis therapy.

העלון לרופא עודכן בספטמבר 2024. להלן העדכונים המהווים החמרה במידע הבטיחותי (מסומנים באדום):

### Black Box Removal

#### ~~WARNING: POTENTIAL RISK OF OSTEOSARCOMA~~

~~In male and female rats, teriparatide caused an increase in the incidence of osteosarcoma (a malignant bone tumor) that was dependent on dose and treatment duration. The effect was observed at systemic exposures to teriparatide ranging from 3 to 60 times the exposure in humans given a 20 mcg dose. Because of the uncertain relevance of the rat osteosarcoma finding to humans, prescribe Terrosa only for patients for whom the potential benefits are considered to outweigh the potential risk. Terrosa should not be prescribed for patients who are at increased baseline risk for osteosarcoma (including those with Paget's disease of bone or unexplained elevations of alkaline phosphatase,~~

~~pediatric and young adult patients with open epiphyses, or prior external beam or implant radiation therapy involving the skeleton) [see Warnings and Precautions (5.1), Adverse Reactions (6.2), and Nonclinical Toxicology (12.1)].~~

## 2 DOSAGE AND ADMINISTRATION

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### 2.4 Administration Instructions

- Administer Terrosa as a subcutaneous injection into the thigh or abdominal region.  
Terrosa is not approved for intravenous or intramuscular use.

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### 2.5 Recommended Treatment Duration

Use of teriparatide for more than 2 years and up to 3 years during a patient's lifetime should only be considered if a patient remains at or has returned to having a high risk for fracture [see Warnings and Precautions (5.1)].

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## 5 WARNINGS AND PRECAUTIONS

### 5.1 Osteosarcoma

An increase in the incidence of osteosarcoma (a malignant bone tumor) was observed in male and female rats treated with teriparatide. Osteosarcoma has been reported in patients treated with teriparatide in the post marketing setting; however, an increased risk of osteosarcoma has not been observed in observational studies in humans. There are limited data assessing the risk of osteosarcoma beyond 2 years of teriparatide use [see Dosage and Administration (2.5), Adverse Reactions (6.3), and Nonclinical Toxicology (12.1)].

Avoid teriparatide use in patients with (these patients are at increased baseline risk of osteosarcoma):

- Open epiphyses (pediatric and young adult patients) (Teriparatide is not approved in pediatric patients) [see Use in Specific Populations (8.4)]
- Metabolic bone diseases other than osteoporosis, including Paget's disease of the bone.
- Bone metastases or a history of skeletal malignancies.
- Prior external beam or implant radiation therapy involving the skeleton.
- Hereditary disorders predisposing to osteosarcoma.

### 5.2 Hypercalcemia and **Cutaneous Calcification**

#### Hypercalcemia

Teriparatide has not been studied in patients with pre-existing hypercalcemia.

Teriparatide may cause hypercalcemia and may exacerbate hypercalcemia in patients with pre-existing hypercalcemia [see Adverse Reactions (6.1, 6.3)]. Avoid teriparatide in patients known to have an underlying hypercalcemic disorder, such as primary hyperparathyroidism.

#### Risk of Cutaneous Calcification Including Calciphylaxis

Serious reports of calciphylaxis and worsening of previously stable cutaneous calcification have been reported in the post-marketing setting in patients taking teriparatide. Risk factors for development of calciphylaxis include underlying autoimmune disease, kidney failure and concomitant warfarin or systemic corticosteroid use. Discontinue teriparatide in patients who develop calciphylaxis or worsening of previously stable cutaneous calcification.

### 5.3 Risk of Urolithiasis

In clinical trials, the frequency of urolithiasis was similar in patients treated with teriparatide and patients treated with placebo. However, teriparatide has not been studied in patients with active urolithiasis. If teriparatide-treated patients have pre-existing hypercalciuria or **suspected/known active urolithiasis**, consider measuring urinary calcium excretion. Consider the risks and benefits of use in patients with active or recent urolithiasis because of the potential to exacerbate this condition.

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### 5.5 Risk of Digoxin Toxicity

Hypercalcemia may predispose patients to digitalis toxicity because teriparatide transiently increases serum calcium. **Consider the potential onset of signs and symptoms of digitalis toxicity when teriparatide is used in** patients receiving digoxin [see Drug Interactions (7.1) and Clinical Pharmacology (11.3)].

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## 6 ADVERSE REACTIONS

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### 6.2 Immunogenicity

**As with all peptides, there is potential for immunogenicity. The detection of antibody formation is highly dependent on the sensitivity and specificity of the assay. Additionally, the observed incidence of antibody (including neutralizing antibody) positivity in an assay may be influenced by several factors, including assay methodology, sample handling, timing of sample collection, concomitant medications, and underlying disease. For these reasons, comparison of the incidence of antibodies in the studies described below with the incidence of antibodies in other studies or to other teriparatide products may be misleading.**

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### 6.3 Postmarketing Experience

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**Adverse Reactions from Observational Studies to Assess Incidence of Osteosarcoma**  
 Two osteosarcoma surveillance safety studies (U.S. claims-based database studies) were designed to obtain data on the incidence rate of osteosarcoma among teriparatide-treated patients. In these two studies, three and zero osteosarcoma cases were identified among 379,283 and 153,316 teriparatide users, respectively. The study results suggest a similar risk for osteosarcoma between teriparatide users and their comparators. However, the interpretation of the study results calls for caution owing to the limitations of the data sources which do not allow for complete measurement and control for confounders.

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## 7 DRUG INTERACTIONS

### 7.1 Digoxin

Sporadic case reports have suggested that hypercalcemia may predispose patients to digitalis toxicity. Teriparatide may transiently increase serum calcium. **Consider the potential onset of signs and symptoms of digitalis toxicity when** teriparatide is used in patients receiving digoxin [see Warnings and Precaution (5.5) and Clinical Pharmacology (11.3)].

## 8 USE IN SPECIFIC POPULATIONS

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### 8.2 Lactation

### Risk Summary

It is not known whether teriparatide is excreted in human milk, affects human milk production or has effects on the breastfed infant. **Avoid Terrosa use in women who are breastfeeding.**

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### **8.4 Geriatric Use**

Of the patients who received teriparatide in the osteoporosis trial of 1,637 postmenopausal women, 75% were 65 years of age and older and 23% were 75 years of age and older. Of the patients who received teriparatide in the trial of 437 men with primary or hypogonadal osteoporosis, 39% were 65 years of age and older and 13% were 75 years of age and older. **Of the 214 patients who received teriparatide in the glucocorticoid induced osteoporosis trial, 28% were 65 years of age and older and 9% were 75 years of age and older.** No overall differences in safety or effectiveness of teriparatide have been observed between patients 65 years of age and older and younger adult patients.

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### **8.6 Renal Impairment**

In 5 patients with severe renal impairment ( $CrCl < 30$  mL/minute), the AUC and T1/2 of teriparatide were increased by 73% and 77%, respectively. Maximum serum concentration of teriparatide was not increased. **It is unknown whether teriparatide alters the underlying metabolic bone disease seen in chronic renal impairment** [see Clinical Pharmacology (11.3)].

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**העלון לצרכן עודכן בספטמבר 2024. להלן העדכונים המהווים החמרה במידע הבטיחותי (מסומנים באדום):**

### **2. לפני השימוש בתרופה**

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- לפני הטיפול בטרזזה, ספר לרופא על כל המצב הרפואי שלך, כולל אם:**
- אתה סובל ממחלת עצמות מסוימת הנקראת פאג'ט (Paget's disease) או ממחלת עצמות אחרת.
  - אתה סובל או שסבלת בעבר מסרטן העצמות.
  - אתה צעיר בשלב הגדילה.
  - עברת טיפול בקרינה.
  - אתה סובל ממצב שקיים במשפחתך שיכול להגדיל את הסיכוי שלך לחלות בסרטן העצמות.
  - יש לך או שהיו לך בעבר רמות גבוהות של סידן בדם (היפרקלצמיה).
  - יש לך או היתה לך תופעה בעור של פצעים כואבים או חבורות שנגרמו מעודף סידן.
  - יש לך או היו לך אבנים בכליות.
  - אתה נוטל תרופות המכילות דיגוקסין.
  - את בהיריון או מתכננת להיכנס להיריון. לא ידוע אם טריפראטייד מזיק לעובר.
  - את מיניקה או מתכננת להניק. לא ידוע אם טריפראטייד מופרש בחלב אם. אין להניק במהלך השימוש בטרזזה.

### **ילדים ומתבגרים**

**לא ידוע האם תרופה זו בטוחה ויעילה בילדים.**  
תרופה זו אינה מיועדת לשימוש בילדים או במתבגרים שהעצמות שלהם עדיין גדלות.

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### **4. תופעות לוואי**

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**טרזזה עלולה לגרום לתופעות לוואי חמורות הכוללות:**

- **סרטן העצמות (אוסטאוסרקומה):** ספר מייד לרופא אם יש לך כאבים בעצמות, כאבים שאינם חולפים באזורים מסוימים בגופך, גושים חדשים או חריגים או נפיחות מתחת לעור הרגישים למגע.
- **עלייה ברמת הסיידן בדם.** ספר לרופא אם יש לך בחילות, הקאות, עצירות, אנרגיה נמוכה או חולשת שרירים. אלה עשויים להיות סימנים לכך שיש יותר מדי סידן בדם שלך.
- **החמרה באבנים בכליות.** אם יש לך או היו לך אבנים בכליות, הרופא עשוי לבדוק את רמות הסיידן בשתן בזמן שאתה משתמש בטרזזה על מנת לראות אם יש החמרה במצב זה.
- **ירידה בלחץ הדם כאשר אתה עובר בין תנוחות.** אנשים מסוימים עשויים לחוש סחרחורת או פעימות לב מהירות מייד לאחר נטילת המנות הראשונות של **טרזזה**. הדבר קורה בדרך כלל תוך 4 שעות מרגע נטילת **טרזזה** ונעלם תוך מספר שעות. עבור המנות הראשונות, השתמש ב**טרזזה** במקום שבו אתה יכול לשבת או לשכב מייד אם אתה חש בתסמינים הללו. אם התסמינים שלך מחמירים או אינם חולפים, פנה לרופא שלך לפני שתמשיך להשתמש ב**טרזזה**.

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