BIOSIDUS

Osteofortil®
Teriparatide

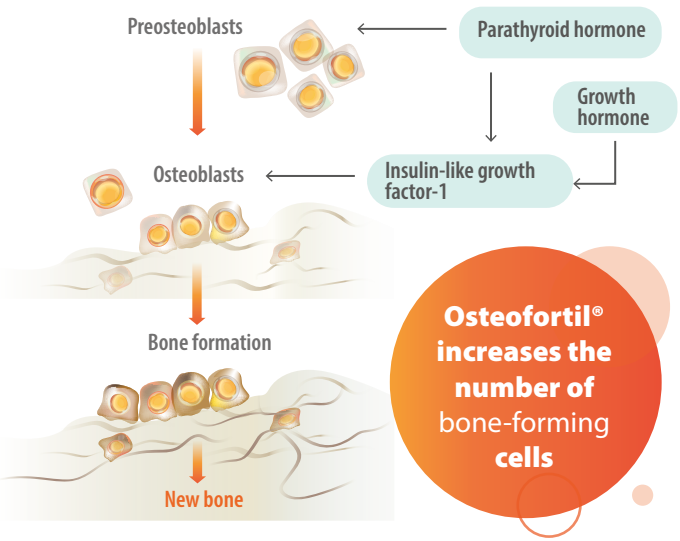
Helping You Enjoy Every Step Of The Way

Osteofortil® Indications[1]

Teriparatide is safe and effective for the treatment of osteoporosis:

- In women with a history of osteoporotic fractures or who are at high risk of fracture.
- In women who failed to or are unable to tolerate conventional therapies for osteoporosis.
- In women over 65 years of age with a T score <-2.5 and previous vertebral fractures.
- Induced by corticosteroids.
- In men with hypogonadal or primary osteoporosis who are at high risk of fracture.

Osteofortil®: The first biosimilar teriparatide with comparative efficacy and safety trials[2,3]



Osteofortil®

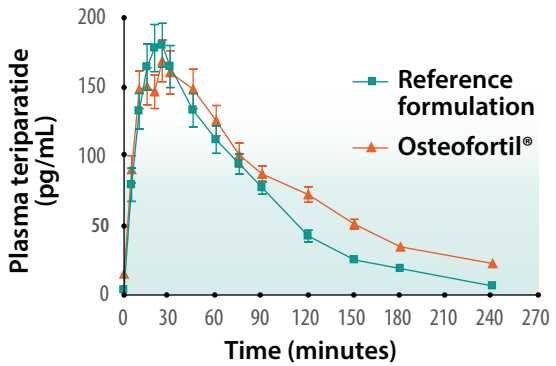
- It is a 34-amino acid peptide identical to the 1-34 fragment of the endogenous human parathyroid hormone (PTH).
- It is produced in *E. coli* using recombinant DNA technology.

Mode of action

- **Teriparatide stimulates bone modeling and remodeling** with a positive effect on mineralization.
  - Increases the number of bone-forming cells. Increases the levels of bone formation and
  - resorption biomarkers. Increases bone formation markers first
  - followed by bone resorption markers (anabolic window).

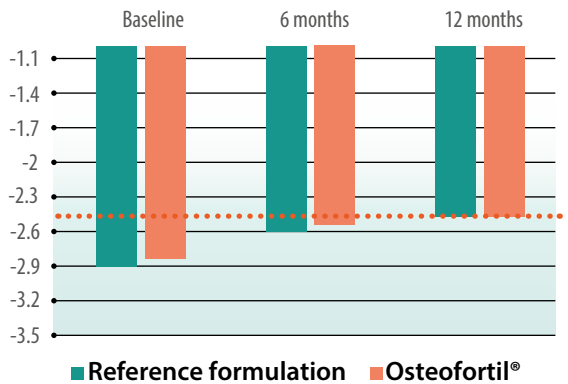
Osteofortil® is interchangeable with the reference formulation since no differences were found in comparability studies[2,3]

Similar relative bioavailability of Osteofortil® *vs* reference formulation



Mean concentration curve in volunteers receiving both formulations

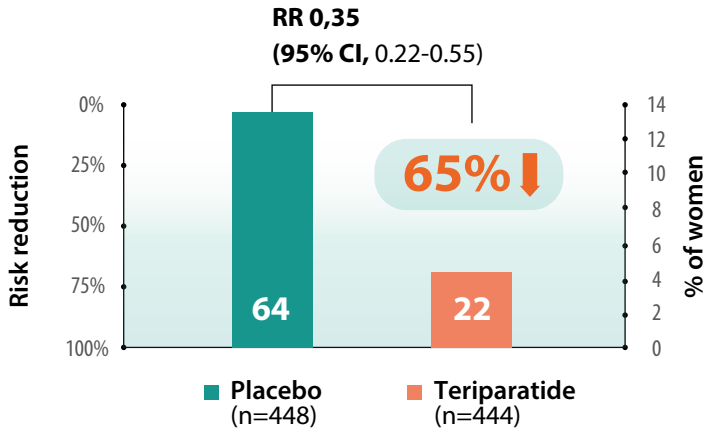
T-score progression in L1-L4



Both formulations demonstrated a comparable safety profile and a similar increase in bone markers.[1,2]

Teriparatide reduces the risk of new vertebral and nonvertebral fractures[4,5]

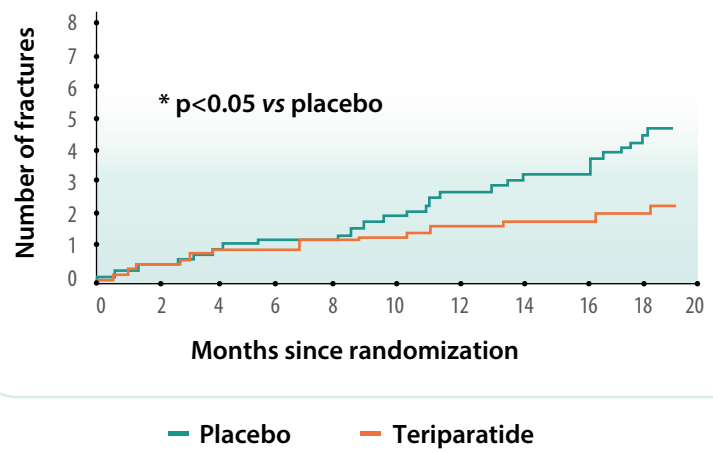
New vertebral fractures[4]



Adapted from Lindsay R. *et al* Sustained vertebral fracture risk reduction after withdrawal of teriparatide in postmenopausal women with osteoporosis. Arch Intern Med. 2004 Oct 11; 164 (18): 2024-30.

65%
reduction in the risk of new vertebral fractures

Nonvertebral fractures[5]



Time to first nonvertebral fracture is shown

Lindsay R, Relationship between duration of teriparatide therapy and clinical outcomes in postmenopausal women with osteoporosis. Osteoporos Int. 2009 Jun;20(6):943-8

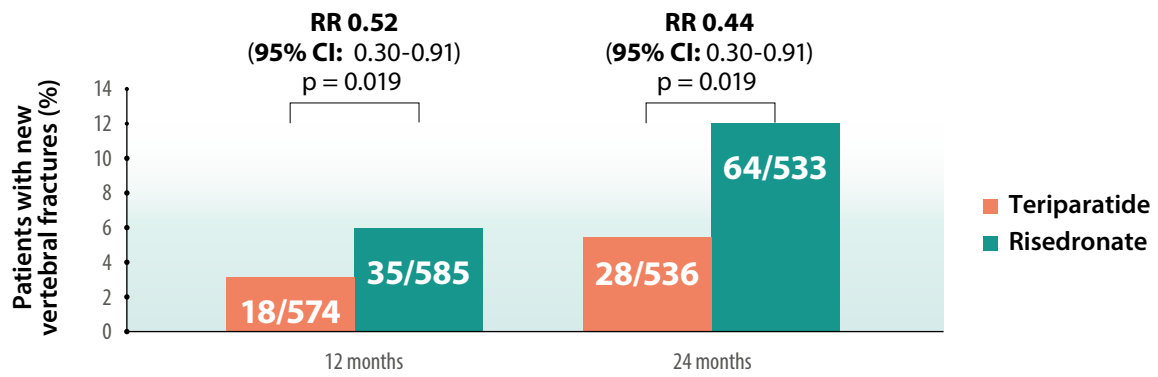
Teriparatide delivers a superior response in postmenopausal women vs bisphosphonates[6]

Reduced incidence of vertebral fractures during 24-month follow-up

	Teriparatide	Risedronate	Effect (95% CI)	p
PrimaryT New vertebral fracture	28 (5%)	64 (12%)	0.44 (0.29-0.68)	< 0.0001
Secondary endpoints Moderate (Q2) or severe (Q3) new vertebral fractures	26 (5%)	63 (12%)	0.42 (0.27-0.65)	< 0.001
Multiple new vertebral fractures	2 (< 1%)	12 (2%)	0.16 (0.04-0.74)	0.007
Nonvertebral (traumatic and fragility) fractures	40 (7%)	57 (9%)	0.70 (0.46-1.05)	0.08

Adapted and modified from Kendler DL *et al* Lancet 2018;391 (10117):230-240.

Incidence of vertebral fractures (teriparatide vs risedronate, 24-month follow-up)



Adapted from Kendler DL *et al* Lancet. 2018;391 (10117):230-240.

↓56% The incidence of new vertebral fractures was reduced by 56%.

↓54% The risk of new and worsened vertebral fractures was reduced by 54%.

Osteofortil®: a reliable option supported by its background and excellent safety profile

Subcutaneous injection in the thigh or abdomen[1]

With or without meals[1]

Maximum efficacy in fracture reduction is achieved at 18-24 months of treatment[7]

Favorable safety profile without increased osteonecrosis of the jaw or atypical fractures, and adequate CV safety in patients with CV history[1]

OSTEOFORTIL®
Product profile

Teriparatide (PTH 1-34)

Active substance

Teriparatide (recombinant DNA technology)	250 µg

Excipientes

Mannitol	45.4 mg
Glacial acetic acid	0.60 mg
Sodium hydroxide q.s	pH = 4.0
Water for injection q.s	1 mL

Store at 2-8 °C.
Avoid direct sunlight.
Keep it in its package.
Keep out of the sight and reach of children.

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Bio es Vida®

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Referencias: 1. Confederación Farmacéutica Argentina. Teriparatida. Available at: https://bit.ly/3c27PUB (accessed july, 2022). **2.** Farias JM *et al.* Initial development of a new teriparatide formulation. *Basic Clin Pharmacol Toxicol* 2014; 115 (Suppl. s1):128. **3.** Farias JM *et al.* Clinical comparison of efficacy of two teriparatide formulations: Osteofortil and Forteo. *Endocrine Reviews*. 2015:12. **4.** Lindsay R *et al.* Sustained vertebral fracture risk reduction after withdrawal of teriparatide in postmenopausal women with osteoporosis. *Arch Intern Med*. 2004 Oct 11; 164 (18):2024-30. **5.** Lindsay R. Relationship between duration of teriparatide therapy and clinical outcomes in postmenopausal women with osteoporosis. *Osteoporos Int*. 2009 Jun;20(6):943-8. **6.** Kendler DL *et al.* Effects of teriparatide and risedronate on new fractures in post-menopausal women with severe osteoporosis (VERO): a multicentre, double-blind, double-dummy, randomised controlled trial. *Lancet*. 2018; 391(10117):230-240. **7.** Silverman S *et al.* The Direct Assessment of Nonvertebral Fractures in Community Experience (DANCE) study: 2-year nonvertebral fragility fracture results *Osteoporos Int*. 2013;24(8):2309-17.

OSTEOFORTIL® - TERIPARATIDE – Solution for injection – Argentine Industry. Prescription-only medicine. **COMPOSITION:** Teriparatide (recombinant DNA origin) solution contains 250 µg/mL (750 µg in each ampoule-vial, 20 µg in each prefilled syringe), mannitol, glacial acetic acid, sodium hydroxide and metacresol (only in vials). **INDICATIONS:** 1. Postmenopausal women with a history of osteoporotic fracture. 2. Patients receiving sustained glucocorticoid therapy (equivalent to 5 mg of prednisone for over 3 months). 3. Postmenopausal women and men with severe osteoporosis (defined as more than one fragility fracture and very low bone mineral density [BMD] (T score <-3.5). 4. Women over 65 years old with a T score <-2.5 and previous vertebral fractures. DOSAGE: The recommended dose of Osteofortil® is 20 µg once daily via subcutaneous injection in the thigh or abdomen. The recommended treatment time of 24 months should not be exceeded. **CONTRAINDICATIONS:** Hypersensitivity to the active substance or to any of the excipients. Pregnancy and breastfeeding. Pre-existing hypercalcemia. Severe renal impairment. Metabolic bone diseases other than primary osteoporosis or glucocorticoid-induced osteoporosis, including hyperparathyroidism and Paget's disease of the bone. Unexplained elevations of alkaline phosphatase. Prior external beam radiation or local radiation therapy to the bones. Patients with bone tumors or bone metastases should be excluded from treatment with teriparatide. **WARNING AND PRECAUTIONS:** Osteofortil® should not be used in: patients who have ever been diagnosed with bone cancer or other cancers that have spread to their bones; patients with Paget's disease of the bone; patients with unexplained high levels of alkaline phosphatase; patients with certain bone diseases (patients should tell their doctor in case of doubt); patients who have had radiation therapy involving their bones. If the patient becomes dizzy after the injection, advise them to sit or lie down until they feel better. If they do not feel better, instruct them to call a doctor before they continue treatment. Advise the patient to take the medicine at the same time each day in order to help them remember their Osteofortil® injections. Osteofortil® may be taken with or without meals. Remind the patient that this medication has been prescribed for their medical condition only and they should not recommend it to others. Carcinogenesis, mutagenesis and impaired fertility: Teriparatide was not genotoxic in a standard battery of tests. Rats treated with near-life time daily injections had dose-dependent exaggerated bone formation and increased incidence of osteosarcoma most probably due to an epigenetic mechanism. Teriparatide did not increase the incidence of any other type of neoplasia in rats. Due to the differences in bone physiology in rats and humans, the clinical relevance of these findings is probably minor. No bone tumors were observed in ovariectomized monkeys treated with teriparatide for 18 months. In addition, no osteosarcomas have been observed in clinical trials or during the post-treatment follow-up study. However, Osteofortil® is contraindicated in patients with primary or secondary bone cancer, and in patients with prior radiation therapy to the bones. Pregnancy: Teriparatide produced no teratogenic effects in rats, mice, or rabbits. No significant effects were observed in pregnant rats administered teriparatide at daily doses of 30-1,000 µg/kg. However, fetal resorption and reduced litter size occurred in pregnant rabbits administered daily doses of teriparatide 3-100 µg/kg. The embryotoxicity observed in rabbits may be related to their higher sensitivity to the effects of PTH on blood ionized calcium compared with rodents. The effect of teriparatide on fertility, pregnancy or breastfeeding is essentially unknown in humans. Although the target population of Osteofortil® are mostly menopausal women, some women receiving Osteofortil® may be of childbearing age (e.g., women treated with corticosteroids). Osteofortil® is contraindicated for use during pregnancy or breastfeeding. Women are encouraged to tell their physician if they are breastfeeding or planning to breastfeed. Women of childbearing age should use effective contraceptive methods during treatment with Osteofortil®. Treatment with Osteofortil® should be discontinued if pregnancy is confirmed. It is not known whether Osteofortil® is excreted in human milk. Pediatric use: The safety and efficacy of Osteofortil® in children has not been established. Osteofortil® should not be used in children (under 18 years old) or growing adults. Geriatric use: The majority of patients receiving Osteofortil® are expected to be menopausal women, more probably of advanced age. A clinical trial evaluating the impact of age on the efficacy of teriparatide examined the response of female patients under and over 75 years old. There were no significant interactions between age and treatment in bone turnover markers, femoral neck BMD, vertebral fractures, nonvertebral fragility fractures, weight loss, hyperuricemia, or hypercalcemia. However, there was an interaction with lumbar spine BMD (explained by authors due to an increase in the placebo arm). The safety assessment showed no interaction between age and treatment. The authors concluded that age does not affect the efficacy and safety of teriparatide in menopausal women with osteoporosis. A European study in 80-year-old women with osteoporosis did not identify any special risk for these patients. Renal and hepatic impairment: Osteofortil® should be used with caution in patients with moderate renal impairment. Osteofortil® must not be used in patients with severe renal impairment. **ADVERSE REACTIONS:** Like all medicines, Osteofortil® may cause side effects in some patients. The most relevant side effects are gastrointestinal disorders, including nausea, reflux, and hemorrhoids, irregular heartbeats, dyspnea, headache, fatigue, asthenia, depression, dizziness, vertigo, anemia, increased sweating, muscle cramps, back pain, myalgia and arthralgia. The most common side effects (affecting more than 10% of treated patients) are general discomfort, headache, dizziness and limb pain. Other side effects that may affect 1-10% of patients include increase in blood cholesterol levels, depression, nerve pain in lower limbs, fainting, irregular heartbeats, increased sweating, muscle cramps, loss of energy, asthenia and precordial pain. The least common side effects (less than 1% of treated patients) are myalgia, arthralgia and edema, mainly in hands and feet, increased heart rate, low blood pressure, heartburn, hemorrhoids, urinary incontinence, pollakiuria, weight gain and injection site reactions. Patients with injection site reactions may experience discomfort such as redness of the skin, pain, swelling, itching, bruising or minor bleeding around the area of the injection; this should clear up in a few days or weeks; otherwise, they should tell their doctor. Elevations of calcium concentrations have been reported in some patients treated with teriparatide. Teriparatide may also cause increased levels of alkaline phosphatase. Some patients (1-10 in every 10,000 treated individuals) have experienced allergic reactions soon after the injection, consisting of breathlessness, swelling of the face, rash and chest pain. **STORAGE AND HANDLING:** Osteofortil® should be kept in the refrigerator (between 2 °C and 8 °C). Osteofortil® vials can be used for 28 days after the first injection, as long as vials are stored in a refrigerator at 2-8 °C. Osteofortil® should not be frozen. Manufactured by: BIOSIDUS S.A., Constitución 4234, (C1254ABX) City of Buenos Aires, Argentina - farmacovigilancia@biosidus.com.ar.

BIOSIDUS
Construyendo un futuro más saludable

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