Prospecto
INGLÉS GENÉRICO

BIOSIDUS

Producto: OSTEOFORTIL® 250 µg		
Tamaño: 280 x 330 mm Material: Papel Obra Primera alisado Gramaje: 50 g/m² (47,5 - 52,5) g/m² Tamaño final doblado: 140 x 41,25 mm (tolerancia máx. 2 mm)	**Código: 153855** **Fecha: 10/2021** Reemplaza a: N/A	Original

Realizado por:	Aprobado por:	Aprobado por:	Aprobado por:	Aprobado por:	Aprobado por:	Aprobado por:
Desarrollo de PKG (Firma y Fecha)	Investigación Clínica (Firma y Fecha)	Control de Calidad (Firma y Fecha)	Comercial (Firma y Fecha)	QA (Firma y Fecha)	Asuntos Regulatorios (Firma y Fecha)	Dirección Técnica (Firma y Fecha)

PANTONE 425 U

BIOSIDUS

OSTEOFORTIL®

TERIPARATIDE (Origin: recombinant DNA)

Injectable solution (S.C.)
Made in Argentina – Sale under filed prescription

COMPOSITION
Each prefilled syringe/VIAL contains:

Teriparatide (rDNA origin), solution	250 µg/ml
Mannitol	45.4 mg
Acetic acid, glacial	0.60 mg
Sodium hydroxide q.s.	pH = 4.0
Water for injection q.s.	1 ml
Metacresol (only in vials)	3.0 mg

DESCRIPTION
OSTEOFORTIL® is an injectable solution supplied in two forms: vial (vial) and pre-filled syringes (see in detail below in section "HOW SUPPLIED").
Each vial (vial) contains 750 µg of teriparatide. Each prefilled syringe contains 20 µg of teriparatide. In both types of presentations, the concentration of teriparatide is the same: 250 µg/mL.

THERAPEUTIC ACTION
Teriparatide is a human parathormone (PTH) analog. The latter is produced in the parathyroid glands, composed of 84 amino acids and has a very important role in the formation of bone in children during growth, as well as in preserving the resistance of the bones in adults, and in maintaining normal levels calcium in blood. Teriparatide, produced in *Escherichia coli* by recombinant DNA technology, is identical to the 34 amino acid N-terminal sequence of endogenous human parathyroid hormone. It performs all the actions of parathormone, which is why it is used to maintain normal calcium levels in patients without parathyroid, to increase bone strength, and to reduce the risk of fractures in people who are at high risk of developing them.
Because of these actions, this product is used mainly for the treatment of osteoporosis. Osteoporosis is a disease that causes the bones to become weaker, brittle, and fractured. This disease, rare in men, is more common in women after menopause. Osteoporosis is also common in patients treated with corticosteroids.

INDICATIONS
OSTEOFORTIL® (teriparatide) is indicated for the treatment of osteoporosis in postmenopausal women with high risk of fracture and in those with severe osteoporosis. This includes women with a history of osteoporotic fractures or who have multiple risk factors for fractures or who have not responded to or are intolerant to prior conventional osteoporotic treatment. In postmenopausal women with osteoporosis, OSTEOFORTIL® (teriparatide) increases bone mineral density and reduces the risk of vertebral and non-vertebral fractures.
OSTEOFORTIL® (teriparatide) is indicated to increase bone mass in men with hypogonadal or primary osteoporosis with high risk of fracture, defined as a history of osteoporotic fracture, the presence of multiple risk factors for fractures, or patients who have not responded or are intolerant to previous conventional osteoporotic therapies. OSTEOFORTIL® increases bone mineral density in men with hypogonadal or primary osteoporosis. The effects of OSTEOFORTIL® in reducing the risk of fractures in men have not been studied.
OSTEOFORTIL® (teriparatide) is indicated for the treatment of osteoporosis associated with sustained systemic glucocorticoid therapy (daily dose equivalent to 5 mg or more of prednisone) in women and men with increased risk of fracture. This is defined as a history of an osteoporotic fracture, the presence of multiple risk factors for fractures, or patients who have not responded to or are intolerant to previous conventional osteoporotic therapies.
OSTEOFORTIL® (teriparatide) is not indicated in pediatric patients or young adults with open epiphyses.

PHARMACOLOGIC PROPERTIES
THERAPEUTIC CLASSIFICATION: ATC code: H05AA02
Mechanism of action
Teriparatide binds to the same receptors as PTH (termed PTHR1 and PTHR2, for parathormone receptor 1 and 2, respectively), with similar affinity and efficacy as PTH. Because of the activation of these receptors, teriparatide produces the same effects as endogenous PTH.
Among the effects, actions on phospho-calcium metabolism and bone function stand out, which are fundamentally mediated by PTHR1. PTH maintains calcium homeostasis, stimulating the release of calcium and phosphate from bone, promoting calcium reabsorption in the kidney and inhibiting phosphate reabsorption there (in the kidney). PTH also increases the synthesis of 1,25-dihydroxy-vitamin D, which, in turn, increases intestinal absorption of calcium and phosphate. The net result of the actions of PTH is an increase in serum concentration of calcium and a reduction in that of phosphate. Prolonged elevation of PTH concentration (e.g., in primary hyperparathyroidism) leads to increased bone resorption, decreased bone mineral density, hypercalcemia, hypercalciuria, and nephrolithiasis. On the contrary, the administration of teriparatide in a single daily injection produces a transitory increase in plasma concentration (with a very short half-life) and in this condition, only the effect of bone anabolism and increased bone mineral density is evidenced.
Pharmacodynamics
Pharmacodynamic properties in menopausal women and men with osteoporosis
OSTEOFORTIL® is a bone-building agent to treat osteoporosis. The effects of OSTEOFORTIL® on the skeleton depend on the pattern of administration. A single daily administration of teriparatide increases the apposition of new bone on the trabecular and cortical bone surfaces (endosteal and periosteal) by preferential stimulation of osteoblasts over osteoclasts. Continuous exposure to endogenous parathormone, on the contrary, modifies the balance of bone turnover with a predominance of bone resorption, which may be detrimental in this pathology.
Pharmacodynamic properties in women and men with glucocorticoid-induced osteoporosis
The action of glucocorticoids at the bone level inhibits bone-forming osteoblastic activity and increases bone resorption.
In controlled clinical studies against an active comparator, in patients with glucocorticoid-induced osteoporosis who received treatment with teriparatide (20 micrograms/day) or alendronate (10 milligrams/day) for 18 months, daily administration of teriparatide stimulated the formation of new bone. Teriparatide also stimulated bone resorption. In these patients, teriparatide also modified the levels of bone turnover markers and serum calcium and phosphorus in a similar way to that observed in studies with postmenopausal women with osteoporosis who did not take glucocorticoids.
Pharmacokinetics
Teriparatide is administered by parenteral route, rapidly passing into the circulation, from where it is eliminated by hepatic and extrahepatic clearance (approximately 62 L/hour in women and 94 L/hour in men). The distribution volume is approximately 1.7 L/kg. The half-life of teriparatide is approximately 1 hour when administered subcutaneously. No metabolism or excretion studies have been performed with teriparatide, but peripheral metabolism of parathyroid hormone is believed to occur predominantly in the kidney and liver.

CLINICAL EFFICACY
Risk factors
Before starting treatment with OSTEOFORTIL®, independent risk factors such as low bone mineral density (BMD), age, personal history of previous fractures, family history of hip fracture, high bone remodeling and low body mass index should be evaluated and considered to identify patients at increased risk of osteoporotic fractures and who could benefit from this treatment.
Postmenopausal women with glucocorticoid-induced osteoporosis should be considered at high risk for fractures if they have prevalent fractures or a combination of risk factors that confer elevated risk of fractures, such as: low BMD (T score ≤ - 2.0), therapy with a high dose of glucocorticoids maintained over time (≥ 7.5 milligrams/day for at least 6 months), low levels of sex steroids, high activity of the underlying disease.
Treatment of menopausal women with osteoporosis
The following effects were observed in a pivotal study that included 1,637 postmenopausal women (mean age 69.5 years), of whom 90% had a history of one or more fractures:
Effect on new vertebral fractures: the administration of teriparatide in conjunction with 1,000 mg of calcium and 400 IU of vitamin D daily, reduced the risk of 1 or more vertebral fractures to 5% compared to 14.3% observed in the group that only received calcium and vitamin D (absolute risk reduction: 9.3%; relative reduction: 65%). Teriparatide was effective in reducing the risk of vertebral fractures regardless of age, bone turnover rate, or BMD at the beginning of treatment.
Effect on non-vertebral fractures: Teriparatide significantly reduced the risk of fractures due to frailty in wrists, ribs, ankle, humerus, hip, foot, pelvis and other sites from 5.5% in the placebo group to 2.6% for the who received teriparatide (absolute risk reduction: 2.9%; relative reduction: 53%).
Effect on BMD: Teriparatide rapidly increased BMD of lumbar spine. Significant increases were observed from 3 months which were maintained throughout the treatment. After a mean treatment period of 19 months, BMD increased by 9% in the lumbar spine and 4% in the hip, with respect to placebo. This increase was independent of age, baseline bone turnover rate, or BMD at the beginning of treatment.
Post-treatment efficacy on fractures: a study included the follow-up of 1262 postmenopausal women for 18 months after termination of teriparatide treatment. Half of the women who received teriparatide and those who received placebo started osteoporosis treatment (without teriparatide), in addition to a daily supplement of calcium and vitamin D. Compared with placebo, the relative risk of new vertebral fractures in women who received teriparatide was reduced by 40%. This relative risk reduction was similar for women receiving or not receiving osteoporosis treatment (41% and 37%, respectively). Regarding the risk of non-vertebral fractures due to frailty, a 42% reduction was observed in women previously treated with teriparatide. These data demonstrate that the risk of fractures decreased in women who received teriparatide, regardless of the treatment subsequently adopted.
Osteoporosis in men
The efficacy of teriparatide administered once-daily was demonstrated in a double-blind, placebo-controlled clinical trial in 437 men (mean age 58.7 years) with hypogonadal or idiopathic osteoporosis. All patients received 1,000 mg of calcium and 400 IU of vitamin D daily for up to 14 months.
In this trial, teriparatide rapidly increased lumbar spine BMD in men, with significant increases as early as 3 months, and continuing throughout treatment. After an average treatment of 12 months, BMD in the spine increased on average by 5% and the hip by 1%, compared to placebo. The increases in BMD were similar among men with hypogonadal or idiopathic osteoporosis, and teriparatide was effective regardless of age, baseline bone turnover rate, and BMD at the start of treatment.
Women and men with glucocorticoid-induced osteoporosis
Glucocorticoid-induced osteoporosis affects both women and men. After the start of glucocorticoid therapy, an early loss of BMD occurs that can continue with sustained therapy.
A 36-month, double-blind, randomized, active comparator (alendronate 10 mg / day) trial demonstrated the efficacy of teriparatide in men and women (N = 428) receiving systemic glucocorticoid therapy (equivalent to a higher dose or equal to 5 mg of prednisone for at least 3 months). This trial included postmenopausal women, premenopausal women, and men. 28% of these patients had a diagnosis of at least one or more vertebral fractures, and all received daily calcium and vitamin D.
Of 69% of patients who completed the first 18-month phase, teriparatide significantly increased lumbar BMD (7.2%) compared to alendronate (3.7%). BMD also increased in total hip (3.6%) and femoral neck (3.7%), compared to alendronate (2.2% and 2.1%, respectively). Furthermore, from 18 to 24 months, the patients treated with teriparatide had an additional increase in BMD at all these points.
When analyzing the X-rays at 36 months, only 1.3% of patients treated with teriparatide had experienced a new vertebral fracture, compared to 7.7% of patients in the alendronate group. A similar number of patients in both groups experienced a non-vertebral fracture.
In premenopausal women, the group treated with teriparatide showed a significantly greater increase in BMD from the start of the trial at 18 months, compared to that of alendronate. However, a significant effect on the fracture rate has not been demonstrated.
The relative effects of teriparatide and alendronate treatment were consistent with subgroups defined by sex, age, body mass index, underlying disease, and other variables.

DOSAGE AND ROUTE OF ADMINISTRATION
Dosage:
The recommended dose of OSTEOFORTIL® is 20 micrograms, administered once a day by subcutaneous injection in the thigh or abdomen.
The total duration of treatment should not exceed 24 months. Patients should not receive more than one 24-month cycle of teriparatide treatment in their lifetime.
In the event of missed dose or inability to inject Osteofortil® at the usual time, the injection should be carried out as soon as possible that same day. Double doses should not be applied to make up for missed doses. Osteofortil® should not be injected more than once on the same day.
Instructions for use:
When the vial presentation is used, the cap of the vial should be cleaned with a wipe or gauze soaked in alcohol, after which 80 microliters of the solution for injection should be extracted with a syringe prescribed by the doctor, which is the volume containing 20 micrograms (recommended daily dose). In case of using the vial presentation, the vial should be stored in the refrigerator immediately after use. A new needle must be used for each injection.
If the prefilled syringe presentation is used, one should be administered daily. To ensure a correct dosage and before carrying out the application, it is recommended to remove the cap covering the needle and, positioning the syringe vertically, with the needle pointing upwards, gently pull the plunger by an amount slightly less than one centimeter. The syringe will then be tapped gently to remove bubbles. Subsequently, and very gently, the plunger should be moved upwards until the first drop is observed. Finally, the injection will be applied.
- Check the expiration date of the medicine. If it has expired, it should not be administered.
- Separate one of the blisters, 30 minutes before administration, out of the refrigerator at room temperature.
- At the moment of administration, we suggest having:
• Cotton pads soaked in alcohol.
• Adhesive band to place on the injection site, after applying the medicine.
• Container to dispose of the material once it has been used.
Steps to follow:
• Wash your hands thoroughly with soap and water.
• Open the blister and place the pre-filled syringe with OSTEOFORTIL® on a flat and clean surface.
• Remove the needle cap.
• Choose the place to inject the medicine, changing it with every application to avoid damaging the skin with successive injections in the same place.
• If you wish, you can keep a written record of the date and place of application for each dose.
• Avoid injecting OSTEOFORTIL® into an area of the body where the skin is irritated or sore.
• With circular movements, clean the skin of the place to be injected with the cotton pad soaked in alcohol.
• Hold the syringe in the hand you will use to inject and hold it between your thumb and forefinger like a pencil.
• With your other hand, hold a fold of skin on the injection area and lift it up with your thumb and index finger.
• Insert the needle at a 90-degree angle, checking that the entire needle has penetrated the skin.
• Let the skin off and with the same hand slightly withdraw the plunger of the syringe.
• If no blood comes out, slowly inject the content of the syringe.
• If blood enters the syringe it means that it entered a small blood vessel, then you should try the application elsewhere.
• After administration of the medicine, remove the needle and press the injection site with a cotton pad for a few seconds. If you wish, you can place an adhesive strip on the area.

Tips for discarding the used material:
• The material supplied is disposable.
• Dispose of the syringe with the needle in a closed container.
• Keep discarded material out of the reach of children.
• Do not dispose of the used material in the household waste bag.
• Ask your doctor or nurse about the best way to dispose of used material.

CONTRAINDICATIONS
- Hypersensitivity to the drug substance or to any of the excipients.
- Pregnancy and breastfeeding.
- Pre-existing hypercalcemia.
- Severe kidney failure.
- Patients with metabolic bone diseases other than primary or corticosteroid-induced osteoporosis, including hyperparathyroidism and Paget's bone disease.
- Unexplained elevations of alkaline phosphatase.
- Patients who have previously received external radiation or radiation therapy localized to the skeleton.
- Patients with bone tumors or bone metastases should be excluded from teriparatide treatment.

WARNINGS AND PRECAUTIONS
Instruct the patient that this product should not be used if they have ever been diagnosed with bone cancer or other types of cancer that have compromised their bones. Nor if have Paget's disease of the bone or have unexplained elevated levels of alkaline phosphatase in the blood. Nor in some other bone diseases, so if in doubt you should consult your doctor. Neither should patients who have received radiotherapy that may have affected their bones receive this product.
Isolated episodes of orthostatic hypotension have been observed, mostly within 4 hours of dosing, resolving spontaneously within minutes to a few hours. This was generally observed after the first administrations, being prevented with the patient lying down. The patient should be recommended that if they become dizzy after an injection, they should sit or lie down until they feel better. In case of not improving, the patient should consult with the doctor before resuming treatment.
To help the patient remember to inject OSTEOFORTIL®, the patient should be instructed to inject at the same time each day. This medicine can also be used at mealtimes, or away from meals, interchangeably.
The patient should be reminded that the drug has been prescribed only for their current medical problem and should not be recommended to others.
No interactions of teriparatide with digoxin were observed, however, it has been mentioned that calcium levels could modify the toxic threshold of digitalis. Use with caution in digitized patients.
Other adverse effects: Increased heart rate, low blood pressure, palpitations.
Treatment duration
Studies in rats showed some cases of osteosarcoma with prolonged treatment with teriparatide. Therefore, until long-term clinical studies are available, treatment with teriparatide should not exceed 24 months of treatment.
Carcinogenesis, mutagenesis and fertility disorders.
Teriparatide was not genotoxic in any of the standard tests.
Rats treated for most of their lives with daily injections exhibited exaggerated, dose-dependent bone formation and an increased incidence of osteosarcoma probably due to an epigenetic mechanism. Teriparatide did not increase the incidence of any other type of neoplasm in rats. Due to the differences in bone physiology in rats and humans, the clinical relevance of these findings is probably low. No bone tumors have been observed in monkeys who had undergone oophorectomy and who were treated for 18 months with teriparatide. Furthermore, no osteosarcoma has been observed during clinical trials or during the post-treatment follow-up study. However, primary or secondary bone cancer, as well as previous bone irradiation, contraindicate the use of OSTEOFORTIL®.
Pregnancy
Teriparatide caused no teratogenesis in rats, mice, or rabbits. No significant effects were observed in pregnant rats receiving teriparatide at daily doses of 30 to 1,000 micrograms/kg. However, pregnant rabbits receiving teriparatide at daily doses of 3 to 100 micrograms/kg

experienced fetal resorption and a reduction in litter size. The embryotoxicity observed in rabbits may be related to their greater sensitivity to the effects of PTH on the calcium ion in the blood, compared to rodents.
The effect of teriparatide on fertility, pregnancy or lactation in humans is essentially unknown. Although most foreseeable users are menopausal women, some may be of childbearing age (for example, women on corticosteroids). Patients are advised not to use OSTEOFORTIL® if they are pregnant or breastfeeding. They are also encouraged to discuss with their physician whether they are breastfeeding or plan to be breastfeeding. Women of childbearing potential must use effective contraception during treatment with OSTEOFORTIL®. If pregnancy does occur, treatment with OSTEOFORTIL® should be stopped. OSTEOFORTIL® is contraindicated in pregnancy.
Breastfeeding
It is unknown whether OSTEOFORTIL® is excreted in human milk. OSTEOFORTIL® is contraindicated during breastfeeding.
Use in pediatrics
Safety and efficacy in children have not been established. OSTEOFORTIL® should not be used in children (under 18 years of age) or in young adults with open epiphyses.
Young adults: There is not enough experience in young adults.
Use in the elderly
It is expected that most patients receiving OSTEOFORTIL® are menopausal women, in many cases elderly. In a clinical study, the impact of age on the effect of teriparatide was evaluated, analyzing the response in women younger than or older than 75 years. No significant interactions between age and treatment were detected in bone turnover markers, bone mineral density in the neck of femur, vertebral fractures, non-vertebral fragility fractures, weight loss, hyperuricemia or hypercalcemia. On the other hand, there was an interaction in bone mineral density in the lumbar spine (explained by the authors by an increase in the placebo group). When evaluating safety, there was also no interaction between treatment and age. The authors concluded that age does not affect the efficacy or safety of teriparatide in menopausal women with osteoporosis. A European study in octogenarians with osteoporosis did not identify any special risk in them.
Use in liver and kidney failure
It is recommended to use with caution in moderate renal dysfunction and avoid it in severe.

ADVERSE REACTIONS
Like any medicine, OSTEOFORTIL® can have adverse effects in some patients. The most relevant are gastrointestinal disorders including nausea, reflux and hemorrhoids, palpitations, dyspnea, headache, fatigue, asthenia, depression, dizziness, vertigo, anemia, increased sweating, muscle cramps, sciatic pain, myalgia and arthralgia.
The most common adverse effects (more than 10% of treated individuals) are malaise, headache, dizziness, and pain in the arms or legs.
In 1% to 10% of patients there is an increase in blood cholesterol levels, depression, neuralgic pain in the lower limbs, fainting, palpitations, sweating, cramps, loss of energy, asthenia and chest pain.
Less frequent adverse effects (less than 1% of treated individuals) include myalgia, arthralgia, and edema mainly of the hands and feet.
Increased heart rate, low blood pressure, heartburn, hemorrhoids, urinary incontinence, frequency, weight gain, reactions at the injection site.
In the case of the latter, some people may experience discomfort such as redness of the skin, pain, swelling, itching, bruising or slight bleeding around the injection site. This usually goes away in a few days or weeks; in case of persistence, medical consultation is required.
Transient elevations of serum calcium have been observed between 4 to 6 hours after injection of teriparatide, returning to baseline values after 24 hours. Routine calcium monitoring is not necessary during treatment. No significant changes in calciuria have been observed in clinical trials.
OSTEOFORTIL® has not been studied in cases of active urolithiasis. Therefore, if used in these cases, it should be done with caution, given the potential risk of worsening calciuria.
Teriparatide can cause an increase in alkaline phosphatase levels.
Some patients (1 to 10 out of 10,000 treated individuals) have experienced allergic reactions immediately after teriparatide injection, consisting of difficulty breathing, swelling of the face, skin rash, and chest pain.

OVERDOSAGE
No cases of untreated overdose have yet been reported. Expected adverse effects of an overdose include nausea, vomiting, dizziness, and headache.
In the event of an overdosage, go to the nearest Hospital or contact the poison control centers.

HOW SUPPLIED
Packages containing 1, 3 and 6 vials with 3 ml of injectable solution (multidose).
Packages containing 30 prefilled syringes with 80 µl of injectable solution.

STORAGE CONDITIONS
OSTEOFORTIL® should be kept refrigerated (between 2º C and 8º C). For the vial presentation, OSTEOFORTIL® can be used for 28 days after the first injection, provided that the vials remain between 2º C and 8º C (in the refrigerator).
OSTEOFORTIL® must not be frozen. Avoid placing the vials or syringes with the product near the freezer to avoid freezing. OSTEOFORTIL® should not be used if it is or has been frozen.
Each vial must be disposed of properly after 28 days of use, even if it is not completely empty.

EN IN CASE OF FREEZING, DISCARD THE PRODUCT.
THIS MEDICINE CANNOT BE PRESCRIBED WITHOUT A NEW PRESCRIPTION.
ITS ADMINISTRATION MUST BE SUPERVISED BY A PHYSICIAN.
KEEP OUT OF REACH OF CHILDREN.

Pharmacovigilance
Report any adverse event to the Drug Safety Unit of **BIOSIDUS S.A.** Constitución 4234 (C1254ABX) Buenos Aires, Argentina (54-11) 4909-8048. farmacovigilancia@biosidus.com.ar

In the event of any inconvenient with the product, please fill out the form available at
http://www.anmat.gov.ar/farmacovigilancia/Notificar.asp
or call ANMAT responde 0800-333-1234.

Medicinal product authorized by the Ministry of Health.
Certificate No.: 56.749
BIOSIDUS S.A.
Constitución 4234, (C1254ABX) Capital Federal.
Manufactured by: Av. Los Quilmes 137, Bernal Oeste, Quilmes, Buenos Aires, Argentina
Technical director: Paula Olcese, pharmacist.

Last reviewed: March 2021

PATIENT INFORMATION LEAFLET

OSTEOFORTIL®

TERIPARATIDE (Origin: recombinant DNA)

Injectable solution (S.C.)
Made in Argentina – Sale under filed prescription

Please read this information before you start taking the medicine, even if you simply have a repeat prescription (or before you start using it and each time you get a repeat prescription). There may be new information, or some information may have changed.

Remember that your doctor prescribed this medicine only for you. Do not administer (or recommend) it to any other person.

This information does not replace talking to your doctor about your disease or treatment.

This medicine must be indicated by your doctor and prescribed by a doctor.

If you experience adverse effects, even if they are not listed in this leaflet, contact your doctor or call 0800-666-2527 (Biosidus S.A. Patient Care Program).

Package contents and composition of OSTEOFORTIL®.
The active ingredient of OSTEOFORTIL® is teriparatide (recombinant DNA).
Each prefilled syringe/vial contains Teriparatide (rDNA origin), solution 250 µg/ml.
Excipients: Mannitol, acetic acid glacial, sodium hydroxide, water for injection and Metacresol (only in vials).

1. ¿ What is the most important information I should know about this product?
OSTEOFORTIL® may cause an increase in the amount of calcium in your blood or urine.
Talk to your doctor before or while in treatment if you:
- Have nausea, vomiting, constipation, and muscle weakness (these may occur because of too much calcium in your blood).
- Have stones, kidney stones or in the ureter.
- Suffer from moderate or severe kidney insufficiency.

Some patients get dizzy or get a fast heartbeat after the first few injections. In that case, **lie down to avoid a fall that could injure you.**
Driving and using machines
You may feel dizzy during treatment, you should not drive or use machines until you feel better.

You should not continue to receive OSTEOFORTIL® after 24 months of treatment.
It should not exceed **two years of treatment in your entire life**.
It should not be used in children or adolescents **under 18 years of age**.
It should not be used in **young people if they are still growing**.

2. What is OSTEOFORTIL® and what is it used for?
OSTEOFORTIL® contains the active substance teriparatide that is used to make the bones stronger, and to reduce the risk of fractures.
OSTEOFORTIL® is used to treat osteoporosis in adults. a disease that causes your bones to become weak. especially common in women after menopause, but it can also occur in men. In addition, osteoporosis can occur in patients on long-term corticosteroid therapy.

3. What should I know before using OSTEOFORTIL® and during treatment?
Who should <u>not</u> use OSTEOFORTIL®?
- If you are allergic to teriparatide or any of the other ingredients.
- If you suffer from high calcium levels (hypercalcemia).
- If you suffer from serious kidney problems.
- If you have or have ever been diagnosed with bone cancer or metastasis (cancer that have spread to your bones)
- If you have a bone disease (tell your doctor).
- If you have high levels of alkaline phosphatase in your blood, that can be caused by a bone disease (Paget's disease).
- If you have received radiation therapy involving your bones.
- If you are pregnant or are planning to be pregnant during treatment.
- If you are breast-feeding.

Pregnancy and breastfeeding:
Do not use OSTEOFORTIL® if you are pregnant of breast-feeding.
If you are under treatment with OSTEOFORTIL®, you cannot get pregnant, so you must use two effective contraceptive methods during treatment.
If you become pregnant, stop treatment with OSTEOFORTIL® immediately.
Can I use OSTEOFORTIL® with other medicines?
Tell your doctor about all the medicines you are taking. This includes:
- Prescription drugs
- Over the counter drugs
- Herbal supplements

These could interfere with the treatment.
Tell your doctor if you receive heart medication, such as digitalis or digoxin.

4. How should I use OSTEOFORTIL®?
The route of administration of this product is subcutaneous.
Use OSTEOFORTIL® exactly as your doctor has told you, at the appropriate times of the day, respecting the dose and duration.
The dose should be applied only once a day, forming a fold in the skin and injecting, rotating the injection site each day, such as thighs and abdomen.
Do not use more than one dose daily.
You can use OSTEOFORTIL® with or without food.
Do not drink alcohol while you are being treated with OSTEOFORTIL®.
Do not change your doses or stop taking OSTEOFORTIL® without first checking with your doctor.
If your child uses OSTEOFORTIL®, the treating physician will decide the correct dosage form and dose, depending on the age and weight of your child.
Store blisters in the refrigerator, do not freeze.
Treatment should not exceed 2 years over your lifetime.
What should I do if I take more doses than usual?
If you used more than the prescribed dose of OSTEOFORTIL®, tell your doctor or contact the poison control center.
The effects of overdose that might be expected include nausea, vomiting, dizziness and headache.
What should I do if I miss a dose?
Do not use more than one daily dose.
If you do not remember to have applied the medication, do not apply the medication that day.
If you are considering stopping treatment, ask your doctor before.

5. What adverse effects can OSTEOFORTIL® cause?
The most common adverse effects are as follows:
Very common: (affects more than 1 patients in 10) General malaise, headache, dizziness and pain in the arms and legs.
Common (affects between 1 to 10 patients in 100): increase in blood cholesterol levels, anemia, depression, neuralgic pain in the legs, sciatic pain, feeling faint, hypotension palpitations, shortness of breath, dyspnea, increased sweating, muscle cramps, loss of energy, fatigue chest pain and gastrointestinal disorders, nausea, reflux.
Uncommon (affects between 1 to 10 patients in 1,000): increased heart rate, low blood pressure, shortness of breath, heartburn (painful or burning sensation just below the breast bone), hemorrhoids, accidental loss or leakage of urine, increased need to urinate, nephrolithiasis, weight gain, injection site reactions, muscle and joint pain, back pain.
Rare: allergic symptoms after injection, lip and facial edema, urticaria, peripheral edema, chest pain.
Changes in complementary tests: increase in alkaline phosphatase, alterations in calcium levels, uric acid levels, weight gain.

Some patients may experience discomfort around the injection site, such as redness of the skin, pain, swelling, itching, bruising, or light bleeding. These should resolve in a few days or weeks. If not, you should tell your doctor as soon as possible. In products of the same pharmacological class, antibodies have been detected in 2.8% of the patients, towards the end of the treatment, which decreased after stopping the treatment.

Contact your doctor immediately if you develop any side effects, even if they are not listed above. You can also contact the National Pharmacovigilance System by calling 0800-333-1234 (ANMAT responde), or Biosidus, calling 0800-666-2527 (Biosidus S.A. Patient Care Program) or the website www.biosidus.com.ar/farmacovigilancia.html.

6. How should I store OSTEOFORTIL®?
OSTEOFORTIL® should be stored in a refrigerator (between 2º C and 8º C) at all times. For the vial presentation, you can use OSTEOFORTIL® for up to 28 days after the first injection, as long as the vials are stored between 2º C and 8º C (in the refrigerator).
Do not freeze OSTEOFORTIL®. Avoid placing the vials or syringes close to the ice compartment of the refrigerator to prevent freezing. Do not use OSTEOFORTIL® if it is or has been frozen.
Each vial should be properly disposed of after 28 days of use, even if it is not completely empty.

7. Further information
This medicine does not contain lactose.

KEEP THIS MEDICINE OUT OF THE SIGHT AND REACH OF CHILDREN.
KEEP THIS MEDICATION REFRIGERATED, DO NOT FREEZE.
DO NOT USE IF THE LIQUID IS TURBID OR HAS SUSPENDED PARTICLES.
BE SURE TO PROPERLY DISCARD THE REMAINS, ONCE APPLIED.

This leaflet summarizes the most important information about OSTEOFORTIL®, for more information and if you have any questions CHECK WITH YOUR DOCTOR.
Do not use this medicine if the label or container is damaged.
You can use OSTEOFORTIL® until the last day of the month indicated on the package. Do not use OSTEOFORTIL® after the expiration date.

In the event of any inconvenient with the product, the patient can fill out the Form at
http://www.anmat.gov.ar/farmacovigilancia/Notificar.asp
or call ANMAT responde 0800-333-1234.

Medicinal product authorized by the Ministry of Health.
Certificate No.: 56.749
BIOSIDUS S.A.
Constitución 4234, (C1254ABX) Capital Federal.
Manufactured in: Av. Los Quilmes 137, Bernal Oeste, Quilmes, Buenos Aires, Argentina
Technical director: Paula Olcese, Pharmacist.

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