

Patient package insert according to Pharmacists' Regulations (Preparations) – 1986

This medicine can be sold with a physician's prescription only

Terrosa[®], solution for injection

Each injected dose contains: teriparatide 20 mcg

Inactive ingredients and allergens in the medicine – see section 6 "Additional information" and in section 2 "Important information about some of the ingredients of the medicine".

Read the entire leaflet carefully before using the medicine. This leaflet contains concise information about the medicine. If you have any further questions, ask the doctor or pharmacist.

You should also read the patient leaflet for **Terrosa Pen**.

This medicine has been prescribed to treat your illness. Do not pass it on to others. It may harm them even if you think that their illness is similar to yours.

Terrosa is a biosimilar medicine. For further information about biosimilar medicines, refer to the Ministry of Health website:

<https://www.gov.il/he/Departments/General/biosimilar>

1. What is the medicine intended for?

- For the treatment of postmenopausal women who suffer from osteoporosis and are at high risk of fracture (defined as having a history of osteoporotic fracture or multiple risk factors for fracture), or who have failed or are intolerant to other available treatments for osteoporosis. In postmenopausal women who suffer from osteoporosis, **Terrosa** reduces the risk of vertebral fractures and non-vertebral fractures.
- For increasing bone mass in men who suffer from primary or hypogonadal osteoporosis and are at high risk of fracture or who have failed or are intolerant to other available treatments for osteoporosis.
- For the treatment of men and women who suffer from osteoporosis associated with systemic and prolonged glucocorticoid treatment (daily dosage equivalent to 5 mg or greater of prednisone) and are at high risk for fracture or who have failed or are intolerant to other available treatments for osteoporosis.

Therapeutic class: calcium homeostasis, parathyroid hormones and analogues.

2. Before using the medicine

Do not use the medicine if:

You are hypersensitive (allergic) to the active ingredient (teriparatide) or to any of the other ingredients the medicine contains (see section 6). Symptoms of a serious allergic reaction to **Terrosa** may include swelling of the face, lips, tongue or throat which may cause breathing or swallowing difficulties. Refer immediately to the doctor or seek urgent medical help if you suffer from these symptoms.

Special warnings regarding the use of the medicine

Terrosa may cause bone cancer: during the testing of the medicine, the medicine caused some rats to develop a bone cancer called osteosarcoma. Studies in humans have not shown that teriparatide increases the chance of developing osteosarcoma. There is little information available about the chance of developing osteosarcoma in patients using teriparatide for more than two years.

Before the treatment with Terrosa, tell the doctor about any medical condition you have, including if:

- You suffer from a certain bone disease called Paget's disease or from another bone disease.
- You suffer or have suffered in the past from bone cancer.
- You are a young person in the growing stage.
- You have undergone radiotherapy.
- You suffer from a condition that exists in your family that can increase your chance of developing bone cancer.
- You have or have had in the past high levels of calcium in the blood (hypercalcemia).
- You have or have had a skin effect involving painful sores or bruises caused by an excess of calcium.
- You have or have had kidney stones.
- You are taking medicines containing digoxin.
- You are pregnant or planning to become pregnant. It is not known whether teriparatide is harmful to the fetus.
- You are breastfeeding or planning to breastfeed. It is not known whether teriparatide is excreted into breastmilk. Do not breastfeed while using **Terrosa**.

Children and adolescents

It is not known whether this medicine is safe and effective in children. This medicine is not intended for use in children or adolescents whose bones are still growing.

Tests and follow-up

During the period of treatment with the medicine, the doctor may check the calcium levels in your urine.

Drug interactions

If you are taking or have recently taken other medicines, including non-prescription medicines and nutritional supplements, tell the doctor or pharmacist. Especially inform the doctor or pharmacist if you are taking or planning to take:

- Medicines containing digoxin – reported cases show that hypercalcemia may cause digoxin toxicity. **Terrosa** may temporarily increase calcium levels. Therefore, consider the signs and symptoms of digoxin toxicity when patients who are taking digoxin are also taking **Terrosa**.

Know the medicines you are taking. Keep a list of them to show the doctor or pharmacist when getting a new medicine.

Use of the medicine and food

The medicine can be injected at any time of the day, regardless of meal times or drinking.

Pregnancy and breastfeeding

Pregnancy

If you are pregnant, think you may be pregnant or are planning to become pregnant, consult the doctor before using this medicine. It is not known whether teriparatide is harmful to the fetus.

Breastfeeding

If you are breastfeeding or planning to breastfeed, refer to the doctor before using this medicine. It is unknown whether teriparatide passes into breastmilk. Do not breastfeed while using **Terrosa**.

Driving and using machines

Using this medicine may cause dizziness (see section 4 "Side effects"). If you experience this, avoid driving or operating machinery.

Important information about some of the ingredients of the medicine

This medicine contains less than 1 mmol sodium (23 mg) per dosage unit, that is to say essentially "sodium-free".

3. How to use the medicine?

Always use the medicine according to the doctor's instructions. Check with the doctor or pharmacist if you are not sure about the dosage and the manner of treatment with the medicine.

The dosage and manner of treatment will be determined by the doctor only.

- Use **Terrosa** exactly as the doctor has instructed you to. The doctor will tell you how much **Terrosa** to use and when to use it.
- Terrosa** cartridges are designed to be used only with the **Terrosa Pen** reusable, multidose medicine delivery system and compatible pen needles. The pen and injection needles are not included with **Terrosa**. However, for treatment initiation a cartridge and pen pack should be used containing one inner carton of **Terrosa** cartridge and one inner carton of **Terrosa Pen**.
- The pen can be used only with injecting needles compatible with the ISO standard for needles for subcutaneous injection, in the following sizes: 29-31 gauge (0.25-0.33 mm diameter) with a length between 5 mm to 12.7 mm.
- Terrosa** is intended for subcutaneous injection. Before the first use, insert the cartridge into the pen. For the correct use of this medicine, it is very important to closely follow the pen's instructions for use, detailed in the User's Manual provided with the pen for injection.
- Before starting to inject **Terrosa** by yourself, the doctor will show you how to use **Terrosa** to inject your dose.
- The usual recommended dosage is one injection of **Terrosa** per day, in the thigh or abdomen (in the lower abdomen area). Do not inject into a vein or muscle. Consult your doctor about how to rotate injection sites.
- Terrosa** has enough medicine for 28 days. **Terrosa** is set to administer a dose of 20 mcg of medicine each day. Do not inject all the medicine in the **Terrosa** cartridge at once.
- Do not transfer the cartridge content to a syringe.
- If you do not have needles to use with **Terrosa Pen**, talk to your doctor.
- Terrosa** should appear clear and colorless. Do not use **Terrosa** if it contains particles, if it is cloudy or colored.
- Inject **Terrosa** immediately after you take the pen with inserted cartridge out of the refrigerator.
- After each use, remove the needle carefully, replace the pen's cap and immediately place the pen with inserted cartridge back into the refrigerator. Do not remove the cartridge from the pen after each use. Store it in the cartridge holder during the whole 28-day treatment period.
- When injecting the first doses of **Terrosa**, make sure you are in a place where you can sit or lie down immediately, in case you experience dizziness or abnormal heartbeat after the injection.
- Do not take more than one injection on the same day.
- Never share your pen with others.
- Do not use **Terrosa Pen** to inject any other medicine (such as insulin). The pen is customised for use with **Terrosa** only. Do not refill the cartridge.
- Do not use **Terrosa** for more than two years over your lifetime, unless the doctor thinks that you need a longer treatment (up to 3 years) because you have high chances of suffering from bone fractures.
- If your doctor recommends calcium and vitamin D supplements, you can take them concomitantly with **Terrosa**.

Preparing the pen for use

- In order to ensure proper administration of **Terrosa**, always read the User's Manual of **Terrosa Pen**, which is enclosed with the pen's carton.
- Wash your hands before handling the cartridge or pen.
- Check the expiry date on the cartridge label before inserting the cartridge into the pen. Make sure there are at least 28 days left before the expiry date. Insert the cartridge into the pen before the first use as detailed in User's Manual of **Terrosa Pen**. Write down the batch number (Lot) of each cartridge and the date of the first injection on a calendar. The date of the first injection should also be recorded on the outer carton package of **Terrosa** (see the intended space on the package: {תאריך שימוש ראשון}).
- After inserting a new cartridge and before the first injection with this cartridge, prime the pen according to the instructions in the User's Manual of **Terrosa Pen**. Do not prime again after injecting the first dose.

Injecting Terrosa

- Before injecting **Terrosa**, clean the skin in the area intended for injection (thigh or abdomen) as the doctor instructed you.
- Gently hold a fold of the cleansed skin and insert the needle straight into the skin. Press on the push button and hold it pressed until the dose indication has returned to the start position.
- After injecting, leave the needle inside the skin for 6 seconds to make sure you receive the whole dose.
- Immediately after you finish the injection, attach the outer needle protective cap to the pen's needle and screw the cap counterclockwise to remove the needle from the pen. This will keep the remaining **Terrosa** sterile and prevent leakage from the pen. It will also stop air going back into the cartridge and the needle from clogging.
- Replace the pen's cap on the pen. Leave the cartridge inside the pen.

For more information on how to use the medicine, visit the website info.terrosa.co.il. The website's password is 2021.

Do not exceed the recommended dose.

If you have accidentally taken a higher dosage, or if a child has accidentally swallowed the medicine, proceed immediately to a doctor or a hospital emergency room and bring the package of the medicine with you. If you take too much **Terrosa**, you may suffer from nausea, weakness/lethargy and low blood pressure. Additional signs, symptoms and complications of an overdose of **Terrosa** may include delayed hypercalcemia effect, vomiting, dizziness and headache.

Continue with the treatment as recommended by the doctor. You should complete the treatment recommended by the doctor. Even if there is an improvement in your health, do not stop taking this medicine without consulting the doctor.

Do not take medicines in the dark! Check the label and the dose each time you take a medicine. Wear glasses if you need them.

If you have further questions on the use of this medicine, consult the doctor or pharmacist.

4. Side effects

Like any medicine, the use of **Terrosa** may cause side effects in some users. Do not be alarmed when reading the list of side effects. You may not suffer from any of them.

Terrosa may cause serious side effects, including:

- Bone cancer (osteosarcoma):** tell the doctor immediately if you have

bone pain, pain that does not go away in certain areas of your body, new or unusual lumps or swelling under the skin that are sensitive to touch.

- An increase in blood calcium level.** Tell the doctor if you have nausea, vomiting, constipation, low energy or muscle weakness. These may be signs that you have too much calcium in your blood.
- Worsening of kidney stones.** If you have or have had kidney stones, the doctor may check the calcium levels in your urine while you are using **Terrosa** in order to see if there is a worsening of this condition.
- Decrease in blood pressure when changing positions.** Certain people may feel dizziness or fast heartbeat immediately after taking the first doses of **Terrosa**. This usually happens within 4 hours of taking **Terrosa** and goes away within a few hours. For the first doses, use **Terrosa** in a place where you can sit or lie down immediately if you feel these symptoms. If your symptoms worsen or do not go away, refer to your doctor before you continue using **Terrosa**.

The most common side effects of Terrosa include:

- Pain
- Nausea
- Joint pain

Side effects observed in studies with postmenopausal women with osteoporosis and men with primary or hypogonadal osteoporosis:

The body in general: pain, headache, weakness, neck pain.

Cardiovascular: hypertension, angina pectoris, temporary loss of consciousness (fainting).

Digestive system: nausea, constipation, diarrhea, indigestion, vomiting, gastrointestinal disorders, dental problems.

Musculoskeletal system: joint pain, leg cramps.

Nervous system: dizziness, depression, insomnia, vertigo.

Respiratory system: rhinitis, increased cough, inflammation of the pharynx, shortness of breath, pneumonia.

Skin: rash, sweating.

Side effects observed in studies with women and men with osteoporosis associated with treatment with corticosteroids:

- Nausea, gastritis
- Pneumonia, shortness of breath
- Insomnia, anxiety
- Herpes zoster

Side effects with unknown frequency that have been observed after marketing of the medicine – it is impossible to reliably estimate their frequency or establish a causal relationship to exposure to the medicine.

- Cases of bone tumor and osteosarcoma have been reported rarely after marketing of the medicine.
- Hypercalcemia: high level of calcium in the blood.

Side effects reported since marketing of the medicine began that were temporarily associated with treatment with teriparatide include:

- Allergic reactions: anaphylactic reactions, hypersensitivity to the medicine, angioedema, hives.
- Laboratory results: increase in the level of uric acid in the blood.
- Respiratory system: severe shortness of breath, chest pain.
- Musculoskeletal system: cramps in the muscles of the legs or back.
- Other: reactions at the injection site, including: pain at the injection site, swelling and bruising; facial edema.

If a side effect occurs, if one of the side effects worsens, or if you suffer from a side effect not mentioned in this leaflet, consult the doctor.

Side effects can be reported to the Ministry of Health by clicking the link "דיווח על תופעות לוואי עקב טיפול תרופתי" found on the homepage of the Ministry of Health website (www.health.gov.il), directing to the online form for reporting side effects or via the link: <https://sideeffects.health.gov.il>

5. How to store the medicine?

- Avoid poisoning! This medicine and any other medicine must be stored in a closed place out of the reach and sight of children and/or infants to avoid poisoning. Do not induce vomiting unless explicitly instructed to do so by the doctor.
- Do not use the medicine after the expiry date (Exp.) stated on the package. The expiry date refers to the last day of that month.
- Storage conditions:** store in the refrigerator at a temperature between 2°C-8°C. Do not freeze. Do not use a preparation that has been frozen. Keep the cartridge in the outer carton package in order to protect from light.
- After the first injection, **Terrosa** can be used for up to 28 days as long as the pen with the cartridge inserted is stored in the refrigerator (2°C-8°C). Do not remove the cartridge from the pen during the 28 days of use.
- Do not use **Terrosa** if it contains particles, if it is cloudy or colored.
- Do not throw away any medicines via wastewater or household waste. Ask the pharmacist how to throw away medicines you no longer use. These measures will help protect the environment.

6. Additional information

In addition to the active ingredient, the medicine also contains:

Mannitol, metacresol, glacial acetic acid, sodium acetate trihydrate, water for injections, hydrochloric acid solution 10%, sodium hydroxide solution 10%.

What the medicine looks like and what the package contains:

- Terrosa** is a clear and colorless solution intended for injection. It is supplied in a cartridge. Each cartridge contains 2.4 ml of solution, which is sufficient for 28 doses.
- One cartridge of 2.4 ml contains 600 mcg of teriparatide (equivalent to 250 mcg per ml).
- Approved package sizes:
A package of **Terrosa**: 1 cartridge or 3 cartridges in a plastic tray packed in a carton.
A package of **Terrosa** cartridge and injection pen: 1 cartridge of **Terrosa** in a plastic tray packed in an inner carton and 1 **Terrosa Pen** packed in an inner carton. The pen is intended for multiple administrations (see the User's Manual of **Terrosa Pen**).

Not all package sizes may be marketed.

Manufacturer name and address: Gedeon Richter PLC., Debrecen, Hungary

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Drug registration number at the national drug registry of the Ministry of Health:

163-82-35787-00

Registration holder: **Dexcel[®] Ltd.**
1 Dexcel St., Or Akiva 3060000, Israel