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

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

Terrosa®, solution for injection

Active ingredient and its quantity: Teriparatide 250 mcg/ml
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 this medicine"

Read this entire leaflet carefully before using this medicine. This leaflet contains concise information about the medicine. If you have any further questions, ask the doctor or pharmacist.
Also read the User's Manual 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 the same as yours.

Terrosa is a biosimilar medicine. For more detailed information regarding biosimilar medicines, see the Ministry of Health website: https://www.health.gov.il/UnitsOffice/HD/MTI/Drugs/Registration/Pages/Biosimilars.aspx

1. What is the medicine intended for?

- Treatment of men and postmenopausal women who are suffering from osteoporosis and are at high risk of developing fractures.
- Treatment of osteoporosis associated with corticosteroid therapy in men and women at increased risk for fractures.
- **Terrosa** increases bone mineral density (BMD), strengthens the bone and reduces the risk for fractures

Therapeutic group: Parathyroid hormones

2. Before using the medicine

Do not use the medicine if:

- You are hypersensitive (allergic) to the active ingredient or to any of the other ingredients this medicine contains (see section 6). Reactions include angioedema and anaphylactic reaction

Special warnings regarding the use of the medicine

- There have been rare reports of osteosarcoma among patients who had been taking teriparatide. In humans, osteosarcoma is a serious but rare cancer. Whether the risk of developing this condition is higher among patients who take **Terrosa** is unknown.
- Duration of treatment is limited to 2 years during a lifetime.

Before the treatment with Terrosa, tell the doctor if:

- You are hypersensitive (allergic) to the active ingredient or to one of the other ingredients of the medicine.
- You suffer, or have suffered in the past, from impaired function of the kidneys/urinary tract, from stones in the kidneys or in the urinary tract or from hypercalciuria.
- You suffer from Paget's disease or from other bone disease.
- You suffer from bones cancer
- You are unable to inject the medicine yourself and there is nobody nearby who can help you with the injection
- You are a child or a young adult who is still in the growing stage
- You have had radiation therapy
- You suffer or have suffered in the past from high calcium levels in the blood or from diseases that cause high levels of calcium in the blood such as hyperparathyroidism.
- You have any other medical condition
- You are pregnant or planning to get pregnant
- You are breastfeeding or planning to breastfeed

Children and adolescents
This medicine is not intended for use in children or in young adults who are still in the growing stage.

Tests and follow-up
During the treatment period with the medicine, your doctor may refer you for blood and urine tests in order to check your response to **Terrosa**. Also, your doctor may ask you to have follow up tests of bone mineral density.

Drug interactions
If you are taking or have recently taken other medicines, including non-prescription medicines and nutritional supplements, tell the doctor or pharmacist. The doctor or pharmacist must be informed in particular if you are taking, or might take:

- Digoxin - **Terrosa** may increase calcium levels. Therefore, extreme care must be taken when using **Terrosa** in patients on Digoxin.

Use of this medicine and food
One may inject at any time of the day, regardless of drink or meals times.

Pregnancy and breastfeeding

- Pregnancy
  There is no available data on teriparatide use in pregnant women to evaluate for drug-associated risk of major birth defects, miscarriage or adverse maternal or fetal outcomes. Discontinuiation of **Terrosa** should be considered when pregnancy is recognized.
- Breastfeeding
  It is not known whether teriparatide is excreted in breast milk, whether it affects breast milk production or has effects on the breastfed infant. Do not breastfeed during treatment with **Terrosa**.

Driving and using machines
Use of this medicine may cause dizziness (see section 4 "Side effects"). In case you experience this, please avoid driving or operating machinery.

Important information about some of the ingredients of this medicine
This medicine contains less than 1 mmol of sodium (23 mg) per dosage unit, that is to say essentially "sodium-free".

3. How to use this medicine

- Always use this 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. The usual recommended dosage is one subcutaneous injection daily, in the thigh or lower abdomen (lower stomach area). Consult your doctor on how to rotate between the injection sites.
- **Do not exceed the recommended dose.**
- The duration of treatment is limited to 2 years during a lifetime.
- This medicine is to be taken at specific time intervals as determined by the attending physician.
- **Terrosa** cartridges are designed to be used only with the **Terrosa Pen** reusable, multidose 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 with injection needles that comply with the ISO standard for needles for subcutaneous injection only in the following sizes: 29-31 gauge (diameter of 0.25-0.33 mm) and 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 instructions for use of the pen which are detailed in the User's Manual provided with the pen for injection.
- **Terrosa** solution for injection should look clear and colorless. Do not use **Terrosa** if it has particles in it, if it is cloudy or colored.
- You can inject **Terrosa** at any hour of the day. To help you remember, it is recommended to inject the medicine at the same time each day.
- Before you try to inject **Terrosa** yourself, the doctor should teach you how to use **Terrosa** so you can inject the medicine in the right way.
- At the beginning of treatment, administer the medicine where you can sit or lie down in case you feel low blood pressure during transition from a reclining to standing position which is characterized by dizziness, weakness, a feeling of fainting and rapid heartbeat.
- Inject the dose immediately after you take the pen with inserted cartridge out of the refrigerator.
  After each use remove the needle with caution, recap the pen and immediately return 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 sleeve during the whole 28-day treatment period.
- Never share your pen with others.
- Do not use your **Terrosa Pen** to inject any other medicine (e.g. insulin). The pen is customised for use with **Terrosa** only. Do not refill the cartridge.
- Do not transfer the content of the cartridge into a syringe.
- Contact your doctor if you do not have needles to use with your **Terrosa Pen**.
- Use the cartridge for 28 days from the first use.
- After a 28 days period, discard the cartridge even if a solution remained in it.
- **Terrosa** has enough medication for 28 days. **Terrosa** is intended to give a dose of 20 mcg of medication each day. Do not inject all the drug in a **Terrosa** cartridge at once.
- Follow your doctor`s instructions about other ways you can treat your osteoporosis, such as exercise, diet and reducing or stopping tobacco and alcohol use. If your doctor recommends calcium and vitamin D supplements, you can take them at the same time you take **Terrosa**.

Preparing the pen for use

- To ensure the correct administration of **Terrosa** always read the User's Manual of **Terrosa Pen**, which is included in the carton of the pen.
- 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 that there are at least 28 days remaining before its 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 its first injection date on a calendar. The date of first injection should also be recorded on the outer carton of **Terrosa** (see the provided space on the box: {תאריך שימוש ראשון}).
- After inserting a new cartridge and before the first injection from this cartridge prime the pen according to the User's Manual of **Terrosa Pen**. Do not prime again after injection of the first dose.

Injecting Terrosa

- Before you inject **Terrosa**, clean your skin where you intend to inject (thigh or lower abdomen) as instructed by your doctor.
- Gently hold a fold of cleansed skin and insert the needle straight into the skin. Press the push button and hold it pressed in until the dose indication has returned to the start position.
- After your injection, leave the needle in the skin for six seconds to make sure that you receive the whole dose.
- As soon as you have finished the injection, attach the outer needle protective cap on the pen needle and screw the cap anti-clockwise to remove the pen needle. This procedure will keep the remaining **Terrosa** sterile and prevent leaking from the pen. This procedure will also stop air going back into the cartridge and the needle from clogging.
- Replace the cap on your pen. Leave the cartridge in the pen.

For additional information on how to use visit the website info.terrosa.co.il. The website password is 2021.

If you accidentally injected a high dose 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. Side effects have been reported namely nausea, vomiting, weakness and dizziness, headache, low blood pressure during transition from lying down to standing up. There may also be an increase in the level of calcium in the blood (hypercalcemia).

If you forgot or if you cannot inject the medicine at the regular time, take it as soon as you can on the same day. **Do not inject Terrosa more than once a day.** Continue with the treatment as recommended by the doctor.
You should complete the treatment as 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:

- Osteosarcoma: Cases of osteosarcoma (bone cancer) and bone tumor have rarely been reported.
- Decrease in blood pressure during transition from a reclining to standing position. Some users feel dizzy, get a fast heartbeat or feel faint right after the first few doses. This usually happens within 4 hours of taking **Terrosa** and goes away within a few hours. For the first few doses, take your injections of **Terrosa** in a place where you can sit or lie down right away if you get these symptoms. If your symptoms get worse or do not go away, stop taking **Terrosa** and call your doctor.
- Increased calcium in the blood.

Tell your doctor if:

- You are experiencing side effects that might indicate high blood calcium levels, such as: nausea, vomiting, constipation, low energy or muscle weakness.

Side effects that appear frequently:

- nausea
- pain
- joints pain

Side effects observed in postmenopausal women and men:

Body as a whole:
Pain, headache, neck pain, asthenia

The heart and blood vessels:
High blood pressure, angina pectoris, temporary loss of consciousness (syncope)

Digestive system:
Vomiting, diarrhea, nausea, constipation, indigestion, teeth problems, gastrointestinal disorders

Musculoskeletal:
Joints pain, leg cramps

Nervous system:
Dizziness, vertigo, insomnia, depression

Respiratory system:
Rhinitis, increased cough, pharyngitis, shortness of breath, pneumonia

Skin:
Rash, sweating

Side effects observed in studies with patients with osteoporosis, associated with corticosteroid therapy:

- nausea
- gastritis
- pneumonia
- dyspnea
- insomnia
- anxiety
- herpes zoster

Side effects with unknown frequency observed after marketing the medicine - their frequency cannot be reliably estimated or causal connection to drug exposure cannot be established.

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

Temporary side effects that have been reported since the start of marketing the drug but are not necessarily causally related to teriparatide treatment include:

- Allergic effects: anaphylactic reactions, drug hypersensitivity, angioedema, urticaria
- Laboratory results: increase in the level of uric acid in the blood
- Respiratory system: severe shortness of breath, chest pain
- Musculoskeletal: muscle spasm of the legs or back
- Others: side effects at the injection site include: injection site pain, swelling, bruising; oro-facial edema

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

Reporting of side effects
Side effects can be reported to the Ministry of Health via the link "דיווח על תופעות לוואי עקב טיפול תרופתי" that can be found on the home page of the Ministry of Health website (www.health.gov.il) directing to the online form of adverse events reporting or via the following link: http://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 2ºC-8ºC. Do not freeze. Do not use the preparation if it has been frozen. Keep the cartridge in the outer carton package in order to protect from light.
- **Terrosa** can be used up to 28 days after the first injection, as long as the pen with cartridge inserted is stored in a refrigerator (2°C-8°C). Do not remove the cartridge from the pen during the 28 days of use.
- Do not use the pen if the solution in the cartridge appears cloudy, colored or has solid particles in it.
- Do not flush medicine down the drain or discard it in the trash. 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, this medicine also contains:
Mannitol, metacresol, glacial acetic acid, sodium acetate trihydrate, hydrochloric acid solution 10%, sodium hydroxide solution 10%, water for injections.

What the medicine looks like and what the package contains:

- **Terrosa** is a colourless and clear solution intended for injection. It is supplied in a cartridge. Each cartridge contains 2.4 mL of solution, enough for 28 doses.
- One cartridge of 2.4 mL contains 600 mcg of teriparatide (corresponding to 250 mcg per mL).
- Approved package sizes:
  Terrosa pack: 1 cartridge or 3 cartridges in a plastic tray packed in a carton.
  Terrosa cartridge and pen pack: 1 **Terrosa** cartridge in a plastic tray packed in an inner carton and 1 **Terrosa Pen** packed into an inner carton. The pen is reusable (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