

Patient leaflet in accordance with the Pharmacists' Regulations (Preparations) - 1986

This medicine is dispensed with a doctor's prescription only

TAKHZYRO
150 mg / 1 ml
Solution for subcutaneous injection in a pre-filled syringe

Composition:

Each pre-filled syringe contains lanadelumab 150 mg in 1 ml solution

Inactive ingredients and allergens in this medicine - see section 2 under 'Important information about some of this medicine's ingredients', and section 6.

Read the entire leaflet carefully before you start using this medicine. This leaflet contains concise information about this medicine. If you have any further questions, consult the child's doctor or pharmacist or nurse. This medicine has been prescribed for your child or a child in your care. Do not pass it on to others. It may harm them, even if it seems to you that their medical condition is similar to yours.

1. WHAT IS THIS MEDICINE INTENDED FOR?

Takhzyro is intended for use in patients 2 years of age and older to prevent recurrent angioedema attacks in patients with hereditary angioedema (HAE).

Therapeutic group: Other hematological agents, medicines used for hereditary angioedema.

What hereditary angioedema (HAE) is

HAE is an inherited condition which runs in families. With this condition the patient's blood does not contain enough of a protein called 'C1 inhibitor', or 'C1 inhibitor' does not work properly. This leads to too high level of plasma kallikrein, which in turn produces higher levels of bradykinin in the patient's bloodstream. Too high levels of bradykinin lead to symptoms of HAE like swelling and pain in the:

- hands and feet
- face, eyelids, lips or tongue
- voice-box (larynx), which may cause difficulty breathing
- genitals.

How Takhzyro works

Takhzyro is a type of protein that blocks the activity of plasma kallikrein. This helps to reduce the amount of bradykinin in the patient's bloodstream and prevents symptoms of HAE.

2. BEFORE USING THE MEDICINE

Do not use this medicine if:

- | |
|---|
| <ul style="list-style-type: none">- your child or the child you are caring for is sensitive (allergic) to the active ingredient – lanadelumab, or to any of the other ingredients of this medicine (see the list of inactive ingredients in section 6). |
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Special warnings regarding use of the medicine

- Talk to the child's doctor, pharmacist or nurse before using Takhzyro.
- If the child has a severe allergic reaction to Takhzyro with symptoms such as a rash, tightness in the chest, wheezing, or a fast heartbeat, tell the child's doctor, pharmacist or nurse immediately.

Children and adolescents

This medicine is not recommended for use in children under 2 years of age as it has not been studied in this age group.

Tests and follow-up

Tell the child's doctor if they are using Takhzyro before having laboratory tests intended to measure how well their blood is clotting. This is because Takhzyro in the blood may interfere with some laboratory tests, leading to inaccurate results.

Drug interactions

If the child is taking or has recently taken other medicines, including non-prescription medicines and nutritional supplements, tell their doctor or pharmacist.

Takhzyro is not known to affect other medicines or be affected by other medicines.

Pregnancy and breastfeeding

If the patient is pregnant or breastfeeding, thinks she is pregnant or is planning to become pregnant, she should ask the doctor or pharmacist for advice before starting to use Takhzyro.

There is limited information on the safety of Takhzyro use during pregnancy and breastfeeding.

As a precautionary measure, it is preferable to avoid the use of lanadelumab during pregnancy and breastfeeding.

Breastfeeding

There is no information about whether lanadelumab is excreted in breast milk. Medicines in this family are excreted in breast milk in the first few days after birth and their level drops afterwards. Therefore, the presence of the medicine in the breast milk in the first few days after birth cannot be ruled out. Lanadelumab may be used during breastfeeding when there is a clinical need.

Driving and using machines

This medicine has no or negligible influence on the ability to drive, ride a bicycle, play near the road or use machines.

Important information about some of this medicine's ingredients

The medicine contains less than 1 mmol sodium (23 mg) per pre-filled syringe; that is to say essentially 'sodium-free'.

3. HOW SHOULD YOU USE THE MEDICINE ?

Takhzyro is provided in single-use pre-filled syringes as ready-to-use solution. The treatment for the child will be started and managed under the supervision of a doctor experienced in the care of patients with HAE.

Always use this medicine according to your doctor's instructions. Check with your doctor or pharmacist if you are not sure about your dose or about how to take this medicine.

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

The recommended dosage is usually:

Adults:

The recommended starting dose is 300 mg every 2 weeks. If you have not had an attack for a long period, your doctor may change the dose to 300 mg every 4 weeks, especially if you have a low body weight.

Adolescents from the age of 12 to 18:

The recommended starting dose is 300 mg every 2 weeks. If you have not had an attack for a long period, your doctor may change your dose to 300 mg every 4 weeks, especially if you have a low body weight.

From the age 6 to 12:

The recommended starting dose is 150 mg every 2 weeks. If the child has not had an attack for a long period, the doctor may change their dose to 150 mg every 4 weeks.

From the age of 2 to 6:

The recommended dose is 150 mg every 4 weeks.

How to inject the medicine

Takhzyro should be injected by a healthcare provider or the child's caregiver. The child's caregiver must carefully read and follow the instructions in section 7, "Instructions for use".

- Takhzyro is intended for injection under the skin ('subcutaneous injection').
- The injection can be given by the medical staff or by the child's caregiver.
- A doctor, pharmacist or nurse should show you how to prepare and inject the medicine properly before you give Takhzyro for the first time. Do not inject until you have been trained to inject the medicine.
- Insert the needle into the fatty tissue in the abdomen, thigh or upper arm.
- Inject the medicine in a different place each time.
- Use each pre-filled syringe of Takhzyro only once.

Do not exceed the recommended dose.**If you have accidentally taken or given a higher dose of Takhzyro than necessary**

If the child has received an overdose or the dose has been given sooner than according to the doctor's prescription, immediately contact a doctor or proceed to a hospital emergency room and bring the package of the medicine with you.

If you forgot to take or give this medicine

If a dose of Takhzyro is missed, inject the dose as soon as possible. The next dose will need to be scheduled according to the frequency so there will be:

- at least a 10-day interval between the doses in patients who receive a dose every two weeks.
- at least a 24-day interval between doses in patients who receive a dose every 4 weeks.

If you are not sure when to inject Takhzyro after a missed dose, ask the child's doctor, pharmacist or nurse.

Adhere to the treatment regimen recommended by the doctor.

The decision to stop using Takhzyro should be discussed with the child's doctor. The symptoms may return upon stopping treatment.

Even if the child feels better, do not stop treatment with this medicine without consulting the doctor.

Do not take medicines in the dark! Check the label and dose each time you take medicine.

Wear glasses if you need them.

If you have any further questions about using this medicine, consult your doctor, pharmacist or nurse.

4. SIDE EFFECTS

As with any medicine, using Takhzyro may cause side effects in some users. Do not be alarmed

when reading the list of side effects; the child may not experience any of them.

If the child has a severe allergic reaction to Takhzyro with symptoms such as a rash, tightness in the chest, wheezing, or a fast heartbeat, **contact your doctor immediately**.

Tell your **doctor, pharmacist or nurse** if you or your child notice any of the following side effects:

Very common side effects (may occur in more than 1 in 10 patients):

- Injection site reactions – symptoms include pain, skin redness, bruising, discomfort, swelling, bleeding, itching, hardening of skin,
- tingling, warmth and rash.

Common side effects (may occur at a frequency of up to 1 in 10 patients):

- Allergic reactions including itching, discomfort and tingling of the tongue
- Dizziness, feeling faint
- Raised skin rash
- Muscle pain
- Blood tests showing liver changes.

If you or your child experience any side effect, if any side effect gets worse, or if you experience a side effect not mentioned in this leaflet, consult your doctor.

Side effects can be reported to the Ministry of Health by clicking on the link “Reporting side effects following drug treatment” found on the Ministry of Health homepage (www.health.gov.il) that directs you to the online form for reporting side effects, or by entering the link: <https://sideeffects.health.gov.il>

5. HOW TO STORE THE MEDICINE?

- Avoid poisoning! This medicine and any other medicine must be kept in a closed place out of the reach and sight of children and/or infants in order 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. date) that appears on the package. The expiry date refers to the last day of that month.

Storage conditions

- Store in a refrigerator (2°C-8°C). Do not freeze. Keep the pre-filled syringe in the original carton package in order to protect from light.
- The pre-filled syringe may be stored below 25°C for a single period of 14 days, but not beyond the expiry date. Do not return Takhzyro to refrigerated storage after storage at room temperature.
- When one pre-filled syringe from a multi-pack is removed from the refrigerator, return the remaining pre-filled syringes to the refrigerator until they are used.
- Throw away the pre-filled syringe if it was not stored in the refrigerator, if it was frozen or not kept in its original carton protected from light.
- **Do not** shake Takhzyro.
- Do not use this medicine if you notice signs of change in the appearance of the medicine such as particles in the pre-filled syringe or changed color of the injection solution.
- Do not throw away any medicines via wastewater or household waste. Ask your pharmacist how to dispose of 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 non-active ingredients: water for injections, L-histidine, sodium chloride, sodium phosphate dibasic (dihydrate), citric acid monohydrate, polysorbate 80

What the medicine looks like and contents of the pack:

Takhzyro is presented as a clear, colorless to slightly yellow solution for injection in a pre-filled syringe.

The pack may contain:

- One pre-filled syringe (1 ml/syringe) in a carton
- Two pre-filled syringes (1 ml/syringe) in a carton
- A pack containing 3 cartons, each carton containing two pre-filled syringes (1 ml/syringe), a total of 6 pre-filled syringes.

Not all pack sizes may be marketed.

Name and address of registration holder and importer: Takeda Israel Ltd., 25 Efal St., Petach Tikva 4951125.

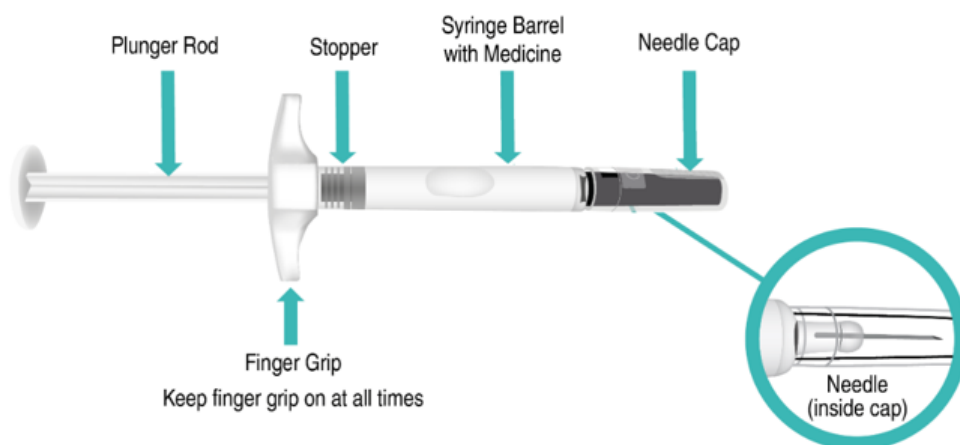
7. INSTRUCTIONS FOR USE

Before injecting Takhzyro, make sure that you read, understand and follow the step-by-step instructions. Contact your child's doctor, pharmacist or nurse if you have any questions.

- **Do not** shake Takhzyro.

Parts of your Takhzyro pre-filled syringe before use (Figure A).

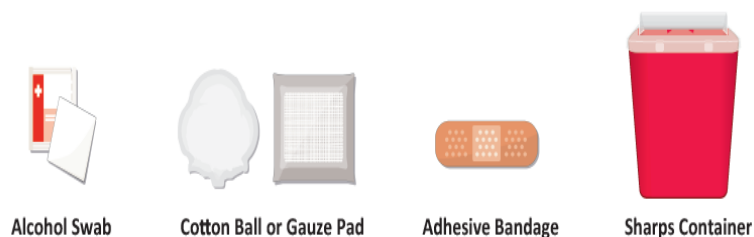
Figure A: Takhzyro pre-filled syringe



STEP 1: Prepare for your injection

- A. Take an alcohol swab, cotton ball/gauze pad, adhesive bandage and a sharps disposal container (**Figure B**) and place on a clean, flat, surface in a well-lit area. These supplies are not included in the Takhzyro packaging.

Figure B: Supplies



- B. Remove the Takhzyro pre-filled syringe carton from the refrigerator 15 minutes before injecting.
- **Do not** use the Takhzyro pre-filled syringe if the tamper evident seal is open or damaged.
 - Your medicine is sensitive to warm temperatures. **Do not** use heat sources such as a microwave or hot water to warm your pre-filled syringe.



- C. Open the carton. Hold the syringe barrel and remove the Takhzyro pre-filled syringe from the tray (**Figure C**).

Figure C: Remove pre-filled syringe



- **Do not** remove the needle cap until you are ready to inject.
 - **Do not** touch or push the plunger rod until you are ready to inject.
- D. Wash your hands with soap and water (**Figure D**). Dry your hands completely.

Figure D: Wash hands



- **Do not** touch any surface or body part after washing your hands before the injection.

E. **Check the expiration date (EXP) on the syringe barrel (Figure E).**

Do not use Takhzyro pre-filled syringe if the expiration date has passed. If the Takhzyro pre-filled syringe is expired, throw it away in a sharps container and contact your doctor, nurse or pharmacist.

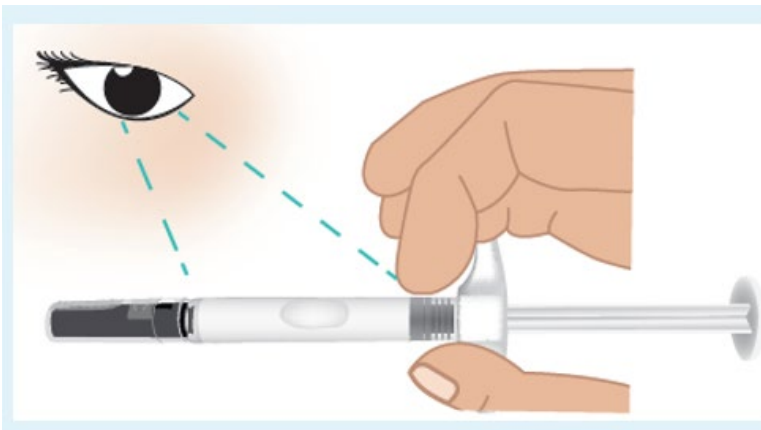
Figure E: Location of expiration date



- **Inspect** the Takhzyro pre-filled syringe for any sign of damage and make sure the medicine is colorless to slightly yellow (**Figure F**).
- **Do not** use product if syringe is damaged – e.g., cracked.
- **Do not** use the Takhzyro pre-filled syringe if the medicine is discolored, cloudy or has flakes or particles in it.
- You might see bubbles in the Takhzyro pre-filled syringe. This is normal and will not affect your dose.

If you cannot use the pre-filled syringe, contact your doctor, nurse or pharmacist.

Figure F: Inspect the pre-filled syringe



STEP 2: Select and prepare your injection site

A. The Takhzyro pre-filled syringe should be injected by the medical staff into the following sites only (**Figure G**):

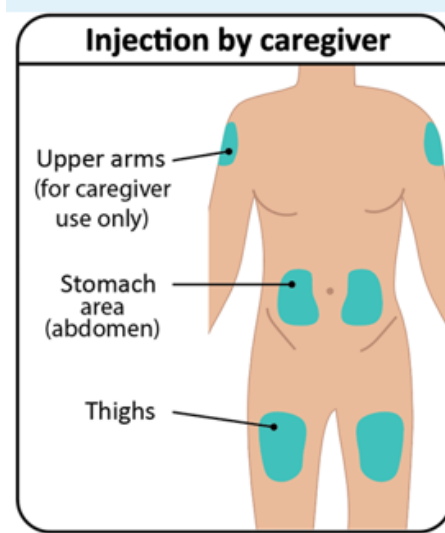
- The upper arm
- Abdomen
- Thigh
- **Do not** inject into an area of the child's body where the skin is irritated, red, bruised or infected.

- The area you choose should be at least 5 cm away from any scars or the child's belly button.

Important:

It is important to inject into different sites to keep skin healthy. Each new injection should be given at least 3 cm from the last injection site.

Figure G: Injection sites



- B. Clean your injection site with an alcohol swab and allow it to dry completely (**Figure H**).
- **Do not** fan or blow air on the clean site
 - **Do not** touch the clean site again before giving your injection.

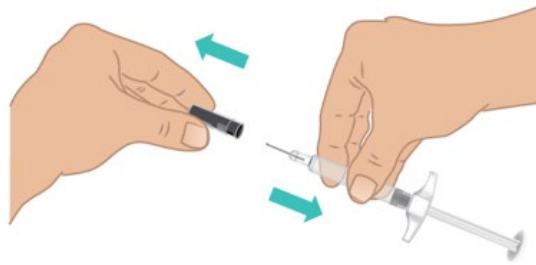
Figure H – Clean injection site



- C. Firmly hold the middle of the Takhzyro pre-filled syringe with one hand, and with the other hand, gently remove the needle cap. (**Figure I**).
- **Do not** touch or push the plunger rod until you are ready to inject.
 - **Do not** use the pre-filled syringe if it has been dropped without the needle cap on.
 - **Do not** use the pre-filled syringe if the needle looks damaged or bent.
 - **Do not** touch the needle or allow the needle to touch anything.

You may see air bubbles in the Takhzyro pre-filled syringe. This is normal. **Do not** try to remove the bubbles.

Figure I – Remove the needle cap



- D. Throw away the needle cap into a sharps container.
- **Do not** recap the needle to avoid needle-stick injury.

STEP 3: Inject Takhzyro

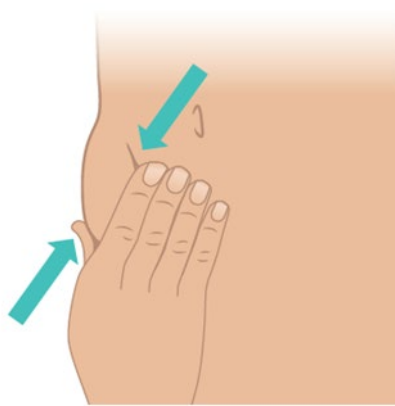
- A. Grip the pre-filled syringe in one hand like a pencil (**Figure J**). Avoid touching the needle or pushing on the plunger.

Figure J: How to grip the pre-filled syringe



- B. With your other hand, gently pinch about 3 cm fold of skin at the cleaned injection site. Keep pinching the skin until the injection is complete and the needle is removed (**Figure K**).

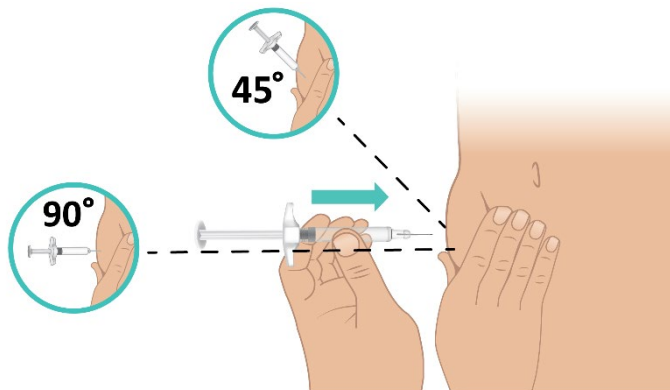
Figure K: Pinch a 3 cm fold of skin



- C. Using a quick, short motion, insert the needle all the way into skin at a 45-to-90-degree angle. Make sure to keep the needle in place (**Figure L**).

Important: Inject directly into the fatty layer under the skin (subcutaneous injection)

Figure L: Insert the needle



- D. Slowly push the plunger **until it stops** (**Figure M**).
- Important:** Do not withdraw the needle until all of the medicine is injected and the syringe barrel is empty. When the injection is complete, you will see the stopper at the bottom of the syringe barrel (**Figure N**).
- E. Slowly withdraw needle while maintaining the syringe at the same angle. Gently release the fold of skin.

Figure M: Push the plunger rod all the way down

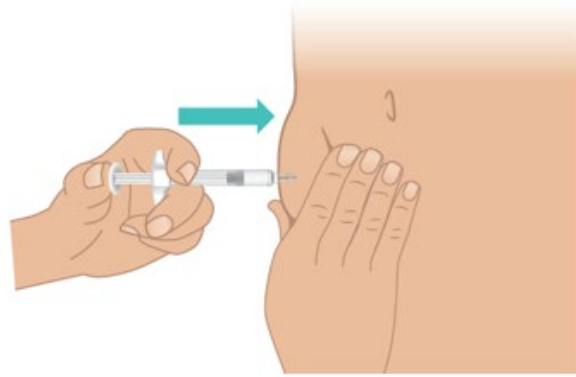
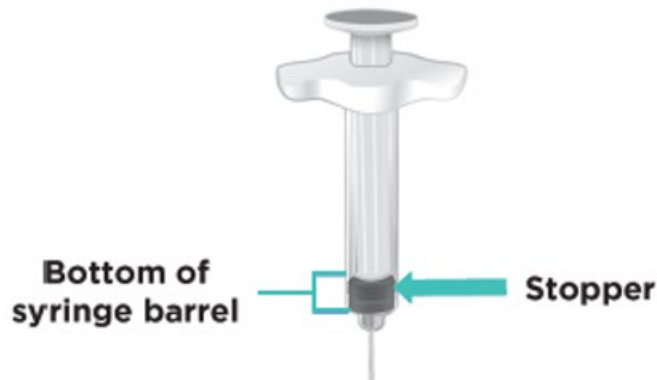


Figure N: Stopper at the bottom of the syringe barrel



- F. Press cotton ball or gauze pad over injection site, if needed, and hold for 10 seconds.
- **Do not** rub the injection site. You may have minor bleeding at the injection site. This is normal.
 - Cover injection site with an adhesive bandage, if needed.

Step 4: Dispose of Takhzyro pre-filled syringe.

- Dispose of your used Takhzyro pre-filled syringe in a sharps disposal container right away after use (**Figure O**)
- **Do not** recap the needle to avoid a needle-stick injury.
- **Do not** reuse the Takhzyro pre-filled syringe or any of your injection supplies.
- **Do not** throw away the pre-filled syringe in your household trash.
- **Do not** touch the needle.

Important: Always keep the sharps disposal container out of the reach of children.

Figure O: Dispose in a sharps container



This leaflet was revised according to the instructions of the Ministry of Health in: March 2024
Registration number of the medicine in the Ministry of Health's National Drug Registry:
163-47-35885-00