PATIENT PACKAGE INSERT IN ACCORDANCE WITH *THE PHARMACISTS' REGULATIONS (PREPARATIONS) – 1986*

This medicine is dispensed with a physician's prescription only

ALPROLIX 250, 500, 1000, 2000, 3000 IU
Powder and solvent for solution for injection

The medicine's name, form and strength:
Each vial of powder contains:

Coagulation factor IX (HUMAN- RFIXFC) 250 IU

Coagulation factor IX (HUMAN- RFIXFC) 500 IU

Coagulation factor IX (HUMAN- RFIXFC) 1000 IU

Coagulation factor IX (HUMAN- RFIXFC) 2000 IU

Coagulation factor IX (HUMAN- RFIXFC) 3000 IU

After being dissolved in water for injection:

1 ml of **ALPROLIX 250 IU** contains approximately 50 IU (250 IU / 5 ml) of Coagulation factor IX (HUMAN- RFIXFC)

1 ml of **ALPROLIX 500 IU** contains approximately 100 IU (500 IU / 5 ml) of Coagulation factor IX (HUMAN- RFIXFC)

1 ml of **ALPROLIX 1000 IU** contains approximately 200 IU (1000 IU / 5 ml) of Coagulation factor IX (HUMAN- RFIXFC)

1 ml of **ALPROLIX 2000 IU** contains approximately 400 IU (2000 IU / 5 ml) of Coagulation factor IX (HUMAN- RFIXFC)

1 ml of **ALPROLIX 3000 IU** contains approximately 600 IU (3000 IU / 5 ml) of Coagulation factor IX (HUMAN- RFIXFC)

Inactive and allergenic ingredients: see section 6 "Additional information" and section 2 "Important information about some of the medicine's ingredients".

Read this leaflet carefully in its entirety before using the medicine. This leaflet contains concise information about the medicine. If you have further questions, consult with your physician or pharmacist.

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

1. What is the medicine intended for?

ALPROLIX is intended for the treatment and prophylaxis of bleeding in patients with hemophilia B (congenital coagulation factor IX deficiency).

Therapeutic group: coagulation factor

ALPROLIX contains the active ingredient human-recombinant coagulation factor IX. Coagulation factor IX is a protein produced naturally in the body, which is needed for the blood to form clots and stop bleeding. **ALPROLIX** is manufactured using recombinant technology, and no human- or animal-derived components are added in the manufacturing process.

In patients with hemophilia B, factor IX is missing or not working properly. **ALPROLIX** is administered to overcome the lack of factor IX.

ALPROLIX increases the level of coagulation factor IX in the blood, and temporarily corrects the bleeding tendency. The structure of the medicine's protein increases the length of time that the medicine works.

2. Before using the medicine

Do not use this medicine if:

- You are sensitive (allergic) to the active ingredient, Coagulation factor IX (HUMAN- RFIXFC), or any of the other ingredients that this medicine contains.

For a list of inactive ingredients, see section 6 “Additional information”.

Special warnings regarding the use of the medicine
Consult with a physician, pharmacist, or nurse before beginning to take ALPROLIX:

- There is a small chance of a sudden severe allergic reaction (anaphylactic reaction) to **ALPROLIX.** Signs of an allergic reaction may include generalised itching, hives, tightness of the chest, difficulty breathing and low blood pressure. If any of these symptoms occur, **stop the treatment immediately** and consult a physician. Due to the risk of an allergic reaction to factor IX, the first **ALPROLIX** treatments should be administered under medical supervision, in a place that provides appropriate medical treatment in case of an allergic reaction.
- Contact your physician if your bleeding is uncontrolled at the dose of **ALPROLIX** that you are taking, as there may be several reasons for this. For example, the formation of antibodies (known also as inhibitors) to factor IX is a known complication that can occur during treatment of hemophilia B. The antibodies prevent the treatment from working properly. This will be checked by your physician. Do not increase the overall dose of **ALPROLIX** to control the bleeding without consulting your physician.

  Patients with a factor IX inhibitor may be at increased risk for anaphylaxis during future treatment with factor IX. For this reason, if you have signs of an allergic reaction like those described above, you should be tested for the presence of an inhibitor.

  Factor IX preparations may increase the risk for formation of unwanted blood clots in your body, especially if you have risk factors for developing blood clots. Symptoms of formation of an unwanted blood clot may include: pain and/or sensitivity along the vein, unexpected swelling of an arm or leg or sudden shortness of breath or difficulty breathing.

Before the treatment with ALPROLIX, tell your physician if:

- You suffer from heart disease or are at risk for heart disease. Extra caution is required while using factor IX.
- If you require a central venous access device (CVAD), risk of CVAD-related complications including local infections, presence of bacteria in the blood and catheter site thrombosis should be considered.

Documentation
It is recommended to record the product’s name and batch number each time **ALPROLIX** is used.

Drug interactions
If you are taking or have recently taken other medicines, including non-prescription medicines and nutritional supplements, inform your physician or pharmacist.

Pregnancy, breastfeeding, and fertility
If you are pregnant or breastfeeding, think you may be pregnant or are planning to get pregnant, consult with a physician before using the medicine.

Driving and using machines
ALPROLIX does not affect the ability to drive or use machines.

Important information about some of the medicine’s ingredients
Sodium – The medicine contains less than 1 mmol (23 mg) of sodium per vial. It is therefore considered to be a “sodium-free” medication. In case of treatment with more than a single vial, the total sodium quantity should be taken into consideration.

3. How should you use the medicine?

This medicine is intended for all ages.
Treatment with **ALPROLIX** will be started by a physician who is experienced in the care of hemophilia patients.
Always use the preparation according to the physician’s instructions. Check with your physician or pharmacist if you are not sure about the dosage or treatment method for this medicine.

ALPROLIX is intended for injection into a vein by yourself or someone else, after receiving appropriate training.

The number of units of coagulation factor IX is expressed in International Units (IU). The dosage and treatment method will be determined by the physician only. Your physician will calculate the required dosage depending on whether treatment is needed for prevention or treatment of bleeding, and depending on your medical condition. Consult with your physician if you think that your bleeding is not controlled by the dosage that you are taking.

Your physician will determine the frequency of treatment depending on the therapeutic response to **ALPROLIX**. Your physician will perform the relevant laboratory tests to confirm that the dosage administered supplies adequate levels of factor IX in your blood.

Treatment of bleeding

The **ALPROLIX** dosage is calculated depending on your body weight and the factor IX levels to be achieved. The target factor IX levels will depend on the severity and location of the bleeding.

Prevention of bleeding

The usual **ALPROLIX** dosage is 50 IU per kg of body weight given once a week or 100 IU per kg of body weight given every 10 days. Your physician may adjust the dose or frequency of administration for you. In some cases, especially in younger patients, shorter dosing intervals or higher doses may be needed.

The elderly

There is limited experience in patients above the age of 65.

Children and adolescents

ALPROLIX can be used in children and adolescents of all ages. In children under the age of 12, higher doses or more frequent injections may be needed. The usual dosage is 50-60 IU per kg body weight given every 7 days.

Do not exceed the recommended dose.

If you have accidentally taken a higher dose, consult with a physician as soon as possible. Always use **ALPROLIX** according to the physician's instructions. Check with your physician or pharmacist if you are not sure about the dosage or method of treatment for this medicine.

If you forget to take the medicine at the scheduled time, do not take a double dose to make up for the forgotten dose. Take the next dose immediately and resume your regular intervals between doses as recommended by your physician. Consult your physician or pharmacist if you are unsure.

Adhere to the treatment regimen as recommended by your physician.

Do not stop treatment with the medicine without consulting your physician.

If you stop using the medicine, you may no longer be protected against bleeding, or a current bleed may not stop.

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

If you have any further questions regarding use of the medicine, consult your physician or pharmacist.

4. Side effects

As with any medicine, the use of **ALPROLIX** may cause side effects in some users. Do not be alarmed by reading the list of side effects. You may not suffer from any of them.

If a sudden severe allergic reaction (anaphylactic reaction) occurs, the injection must be stopped immediately.

Contact your physician immediately if any of the following symptoms of allergic reaction appears: swelling of the face, rash, generalised itching, hives, tightness of the chest, difficulty breathing, burning and stinging at the injection site, chills, flushing, headache, general feeling of being unwell, nausea, restlessness, rapid pulse and low blood pressure.

In children who have not previously been treated with preparations containing factor IX, the effect of inhibitor formation (see section 2 "Special warnings regarding the use of the medicine") is common (occurs in 1-10 users out of 100). In this case, the medicine may stop working properly, and your child may suffer from persistent bleeding. If this happens, you must consult the physician immediately.

The following side effects may occur with the medicine.

Common side effects – effects that occur in 1-10 users out of 100:

Headache, lack of sensation or tingling in the mouth, flank pain along with blood in the urine (obstructive uropathy) and redness at injection site. In children not previously treated with factor IX medicines: formation of factor IX inhibitors, hypersensitivity.

Uncommon side effects – effects that occur in 1-10 users out of 1,000:

Dizziness, taste alterations, bad breath, tiredness, pain at injection site, rapid pulse, blood in the urine (hematuria), flank pain (renal colic), low blood pressure and decrease in appetite.

Side effects with unknown frequency (effects for which their frequency has not yet been determined):

A sudden, severe, life-threatening allergic reaction (allergic shock, anaphylactic shock).

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 your physician.

Side effects can be reported to the Ministry of Health by clicking the link "Report adverse effects associated with medications" on the homepage of the Ministry of Health website (www.health.gov.il), which will direct you to the online form for reporting side effects, or by entering the link: https://sideeffects.health.gov.il

5. How should the medicine be stored?

- Avoid poisoning! This medicine and any other medicine should 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 physician.
- 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. Do not use medicine that has been stored out of the refrigerator at a temperature of up to 30ºC for over 6 months.

Storage conditions:

- Store in a refrigerator (2°C - 8°C). Do not freeze.
- Store in the original package in order to protect the preparation from exposure to light.
- During its shelf life, the medicine can be kept at a temperature of up to 30ºC for a single period of up to 6 months. After removal from refrigeration, it cannot be returned to the refrigerator. Do not use past the expiry date or 6 months after removing from refrigeration, whichever is earlier. The date that it was removed from the refrigerator and stored at room temperature must be marked on the package.
- Use the preparation straight away after preparing it (dissolving the powder). If the preparation cannot be used straight away, it should be used within 6 hours at storage conditions of up to 30°C. Do not store the prepared solution in the refrigerator. Protect the prepared solution from direct sunlight. The prepared solution should be destroyed after 6 hours if it has not been used. According to microbial considerations – the preparation should be used straight away after being dissolved.
- The prepared solution will be clear to slightly pearl-like (opalescent) and colourless. Do not use the medicine if you notice that it is cloudy or contains visible particles.

- The preparation is intended for single use only.
- Discard any unused remnants of the solution. Do not throw away 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, Sucrose, Histidine, Polysorbate 20, Sodium hydroxide (for pH adjustment) and Hydrochloric acid (for pH adjustment).

  Solvent: 5 ml Sodium chloride and water for injection

  If you are on a low-sodium diet, see section 2 “Important information about some of the medicine’s ingredients”.

- **What the medicine looks like and contents of the package:**

ALPROLIX is sold as a powder and solvent for preparation of a solution for injection.

The powder is white to off-white in color, in a vial.

The solvent is a clear, colorless solution, in a pre-filled syringe.

After the powder is dissolved, the solution obtained is clear to slightly pearl-like (opalescent) and colorless.

Each pack of **ALPROLIX** contains a vial of powder, a syringe pre-filled with solvent, a plunger rod, a vial adapter, an infusion set, 2 alcohol swabs, 2 plasters and a gauze pad.

The items needed for preparation and injection of the solution are supplied in each pack of the preparation.

- **Registration holder and address:** MegaPharm Ltd., 15 Ha’tidhar Street, Ra’anana, Israel.
- **Manufacturer name and address:** Swedish Orphan Biovitrum AB (SOBI), Stockholm, Sweden.
- Revised in May 2024.
- Registration number of the medicine in the Israeli Drug Registry of the Ministry of Health:

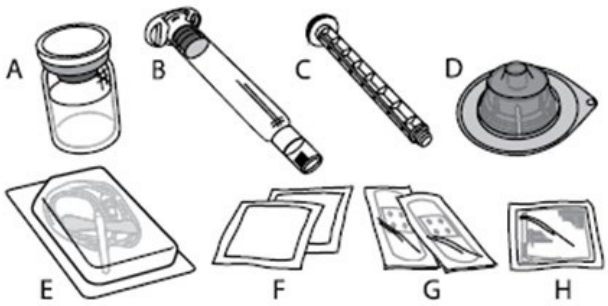
  ALPROLIX 250 IU 171-47-37091-00
  ALPROLIX 500 IU 171-48-36890-00
  ALPROLIX 1000 IU 171-49-36891-00
  ALPROLIX 2000 IU 171-50-36892-00
  ALPROLIX 3000 IU 171-51-36893-00

Detailed instructions for the preparation and injection of ALPROLIX

The instructions below describe how to prepare and use **ALPROLIX**. Please read these instructions in their entirety before using **ALPROLIX**.

ALPROLIX is administered by intravenous injection after being dissolved in the solvent supplied in the pre-filled syringe. Each pack contains:

1 powder vial (**A**)
5 ml solvent in pre-filled syringe (**B**)
1 plunger rod (**C**)
1 vial adaptor (**D**)
1 infusion set (**E**)
2 alcohol swabs (**F**)
2 plasters (**G**)
1 gauze pad (**H**)



Do not mix this medicine with other solutions for injection or infusion.

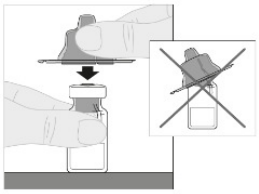
Wash your hands before opening the pack.

Preparation:

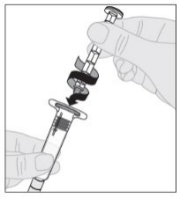
1. Check the name and strength on the package, to make sure it contains the correct medicine. Check the expiry date on the carton package. Do not use if the expiry date that appears on the package has passed.
2. If **ALPROLIX** has been stored in a refrigerator, allow the vial of **ALPROLIX** (**A**) and the syringe with solvent (**B**) to reach room temperature before use. Do not use an external heat source.
3. Place the vial on a clean flat surface. Remove the plastic cap from the vial.

4. Wipe the top of the vial with one of the alcohol swabs (**F**) provided in the pack, and allow to air dry before using. **Do not** touch the top of the vial and **do not** allow any surface or object to touch the top of the vial once it has been wiped.

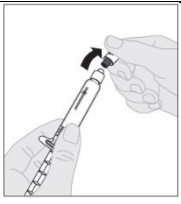
5. Peel back the protective paper lid from the vial adapter (**D**). **Do not** remove the adaptor from its plastic wrapping. **Do not** touch the inside part of the adaptor's package.
6. Place the vial on a flat surface. Hold the vial adapter with its plastic wrapping and place it perpendicular to the top of the vial. Press down firmly until the adapter snaps into place on the vial opening, with the adapter spike penetrating the vial stopper.



7. Attach the plunger rod (**C**) to the solvent-filled syringe by inserting the tip of the plunger rod into the opening in the syringe plunger. Turn the plunger rod firmly clockwise until it is properly attached to the syringe.

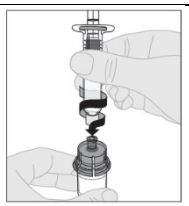


8. Hold the syringe barrel, and break the white plastic cap at the syringe tip by bending the cap until it breaks off. Set the cap aside by placing it, top down, on a flat surface. **Do not** touch the inside part of the cap or the syringe tip.

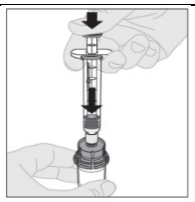


9. Remove the adaptor's wrapping and discard in the waste bin.

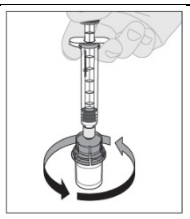
10. Connect the solvent syringe to the vial adapter by inserting the tip of the syringe into the adapter opening. Firmly push the syringe and turn it clockwise until it is properly connected.



11. Slowly depress the plunger rod to inject all the solvent into the powder vial.



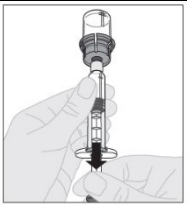
12. With the syringe still connected to the adapter and the plunger rod pressed down, **gently** swirl the vial until all the powder is dissolved. **Do not** shake.



13. Visually inspect the solution obtained before use. The solution should appear clear to slightly pearl-like (opalescent) and colourles. Do not use the solution if it is cloudy or contains visible particles.

14. Ensuring that the syringe plunger rod is still fully pressed down, invert the vial. Slowly pull on the plunger rod to draw back all the solution through the vial adapter into the syringe.

    Note: if you use more than one vial of **ALPROLIX** for each injection, each vial should be prepared separately as per the instructions described above (steps 1-13). Remove the solvent syringe, and leave the vial adapter in place. A single large luer lock syringe may be used to draw back the prepared solution from each of the individual vials.



15. Detach the syringe from the vial adapter by pulling and gently turning the vial counterclockwise.

16. Discard the vial and the adapter.

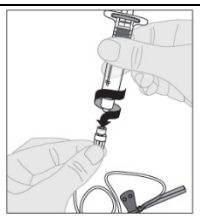
Note: If you do not use the solution immediately, carefully return the syringe cap to the tip of the syringe. Do not touch the syringe tip or the inside of the cap.

After preparation, **ALPROLIX** may be stored at room temperature, protected from direct sunlight, for up to 6 hours.
After 6 hours, the prepared solution should be discarded.

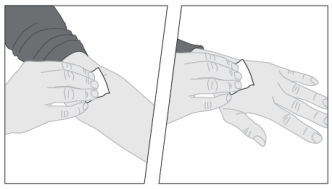
Administration (intravenous injection):

Use the infusion set (**E**) provided in the pack.

1. Open the infusion set package and remove the cap at the end of the tubing. Attach the syringe with the prepared solution to the end of the infusion set tubing by turning clockwise.



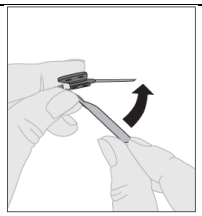
2. Apply a tourniquet if needed and prepare the injection site by cleansing the skin with the second alcohol swab provided in the pack.



3. Remove any air in the infusion set tubing by slowly pressing the plunger rod until the liquid reaches the infusion set needle. Do not push the solution through the needle. Remove the clear plastic protective cover from the needle.

4. Insert the infusion set needle into a vein as instructed by your physician or nurse and remove the tourniquet. If you prefer, you may use one of the plasters (**G**) provided in the pack to hold the plastic wings of the needle in place at the injection site. Inject the prepared solution into the vein over several minutes. Your physician may change your recommended injection rate depending on the level of comfort that you experience.

5. After performing the intravenous injection of the preparation and removing the needle, fold the needle protector over and attach it to the needle.



6. The used needle, any unused solution, the syringe and the empty vial should be disposed of in an appropriate medical waste container, as these items may harm others if not properly disposed of.