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

The medicine is dispensed with a doctor's prescription only

RECORMON®

4,000 IU/0.3 ml
5,000 IU/0.3 ml
6,000 IU/0.3 ml
10,000 IU/0.6 ml
30,000 IU/0.6 ml
Pre-filled syringe

Composition:
Each pre-filled syringe contains:
epoetin beta.
Inactive ingredients and allergens: See section 2 under "Important information regarding some of the ingredients of the medicine" and section 6 - "Further Information".

Read this leaflet carefully in its entirety before using the medicine. This leaflet contains concise information about the medicine. If you have further questions, refer to the doctor or pharmacist.
- Keep this leaflet. You may need to read it again.
- This medicine has been prescribed to treat your ailment. Do not pass it on to others. It may harm them even if it seems to you that their medical condition is similar.

If the side effects worsen, or if you notice side effects that are not mentioned in this leaflet, refer to your doctor or pharmacist.

Important information for your review
- Strictly follow the doctor's instructions (dosage and duration of treatment). Failure to strictly follow them may impair the effectiveness of the treatment. Never stop treatment without consulting your doctor. Please read sections 2 and 4 for detailed safety information.
- The medicine is intended for subcutaneous (under the skin) or intravenous injection, and is provided in a single use pre-filled syringe. If you are injecting the medicine to yourself, follow the self-injection instructions detailed at the end of the leaflet. During the course of treatment, perform periodic blood and blood pressure tests.
- It is recommended that iron supplements should be taken during the course of treatment.
- Store the medicine in the refrigerator, at a temperature between 2-8°C and keep the syringes in the original package in order to protect from light.

1) WHAT IS THE MEDICINE INTENDED FOR?

Recormon is intended:
- For treatment of anemia caused by chronic renal failure in dialysis patients and in patients not dependent on dialysis.
- For treatment of anemia in adult cancer patients receiving chemotherapy.
- For treatment of patients requiring an autologous blood transfusion before surgery. The epoetin beta injections will increase the amount of blood that will be taken from your body before surgery and later returned to your body during or after the surgery (autologous transfusion).

Therapeutic group:
Synthetic recombinant erythropoietin
Recormon is a clear, colorless solution for injection under the skin or intravenously. It contains a hormone called epoetin beta, which stimulates the production of red blood cells. Epoetin beta is produced by a genetic technology and works in exactly the same way as the natural hormone erythropoietin.

2) BEFORE USING THE MEDICINE

Do not use the medicine if:

- you are hypersensitive (allergic) to epoetin beta or to any of the additional ingredients contained in the medicine (see section 6 - "Further Information").
- you suffer from uncontrolled blood pressure.
- you are due to donate blood for yourself before surgery, and:
  - you suffered from a heart attack or stroke in the month before treatment.
  - you have suffered or suffer from unstable angina pectoris - new or increasing chest pain.
  - you are at risk of deep venous thrombosis - for example, if you have had blood clots in the past.

If any of these apply to you, or might apply, tell your doctor at once.

Special warnings regarding the use of the medicine

Before treatment with Recormon, tell the doctor if:
- your anemia did not improve with epoetin beta treatment
- you suffer from a deficiency of certain B vitamins (e.g., folic acid or vitamin B12)
- you have very high blood levels of aluminum
- your blood platelet count is high
- you suffer from a chronic liver disease
- you suffer from epilepsy
- you have developed anti-erythropoietin antibodies and Pure Red Cell Aplasia (PRCA) (a condition in which red blood cell production is reduced or fully stopped) during prior exposure to other medicines from the erythropoietin family. In this case, do not switch to treatment with **Recormon**.

Take special care with other medicines that stimulate red blood cell production:
Recormon belongs to a group of medicines that stimulate the production of red blood cells in a process identical to the natural process in the body. Your doctor will record the exact name of the medicine you are using.

Serious skin reactions including Stevens-Johnson syndrome (SJS) and toxic epidermal necrolysis (TEN) have been reported in association with epoetin treatment.

These serious skin reactions (SJS/TEN) can appear initially as reddish lesions (target-board-like lesions) or circular patches, often with central blisters on the body. Also, ulcers of mouth, throat, nose, genitals and eyes (red and swollen eyes) can occur.

These serious skin rashes are often preceded by fever and/or flu-like symptoms. The rashes may progress to widespread peeling of the skin and life-threatening complications.

If you develop a serious rash or another of these skin symptoms, stop taking **Recormon** and contact your doctor or seek medical attention immediately.

Special warnings during the course of treatment with Recormon:
Tell your doctor if you do not feel better or if you feel worse while using the medicine.

If you suffer from a chronic kidney disease, and particularly if you do not respond properly to **Recormon**, the attending doctor will check the **Recormon** dosage that you are receiving, since repeated increases in dosage, if you do not respond to treatment, may increase the risk of heart function or blood vessel problems and may increase the risk of myocardial infarction, stroke and death.

If you are a cancer patient, you should be aware that **Recormon** may act as a factor that stimulates blood cell proliferation and in some circumstances, may have a negative impact on your cancer. Depending on your individual situation, a blood transfusion may be the preferable treatment for you. Your doctor will make this decision.

If you have nephrosclerosis and you are not on dialysis, your doctor will decide whether treatment with **Recormon** is suitable for you. This is because acceleration of progression of kidney disease cannot be ruled out with absolute certainty.

If you suffer from a chronic kidney disease and are on dialysis, it may be necessary to change the heparin dosage, to prevent blockage of the tubing of the dialysis system.

If you suffer from chronic kidney disease and being treated with dialysis and are at risk of shunt (a vessel that enables connection to the dialysis system) thrombosis, blood clots (thromboses) may form in the shunt. Your doctor may decide to give you aspirin (acetylsalicylic acid) or modify the shunt.

If you are due to donate blood to yourself before surgery, the attending doctor will make sure to check:
- that you are suitable for donating blood, especially if your weight is less than 50 kg.
- that you have a sufficient level of red blood cells (your hemoglobin is at least 11 g/dL).
- that only 12% of your blood volume will be donated at once.

Recormon is not suitable for use by healthy people, since it may lead to an increase in blood cells, to increased thickness of the blood and consequently cause life-threatening complications of the heart and blood vessels.

Tests and follow-up
Your doctor will carry out regular blood tests to monitor how your anemia is responding to treatment by measuring your hemoglobin level.
In addition, during the course of treatment with this medicine, your doctor may perform regular blood tests to check:
- Your potassium levels. If you have high or rising potassium levels, your doctor may reconsider the treatment.
- Blood platelet count. Epoetin beta treatment may lead to a mild to moderate increase in platelet counts, which may cause changes in blood clotting.

Interactions with other medicines
If you are taking, or have recently taken, other medicines, including non-prescription medicines and nutritional supplements, tell the doctor or pharmacist.

Use of the medicine and food
If you are sensitive to any food or medicine, inform the doctor before taking this medicine.

Pregnancy, breast-feeding and fertility
If you are pregnant or breast-feeding, consult a doctor or pharmacist before using medicines.
There is not much experience in treating pregnant or breast-feeding women with **Recormon**. There is no evidence that **Recormon** causes impaired fertility in animals. The potential risk in humans is unknown.

Driving and using machines
This medicine has no known effect on the ability to drive or operate machines.

Important information regarding some of the ingredients of the medicine
This medicine contains phenylalanine and may be harmful to patients suffering from phenylketonuria **(PKU)**.
If you suffer from phenylketonuria, consult a doctor regarding treatment with **Recormon**.
This medicine contains less than 1 mmol sodium (23 mg) per dose, i.e., **Recormon** is essentially 'sodium-free'.

3) HOW SHOULD YOU USE THE MEDICINE?

Always use this medicine according to the doctor's instructions.
Check with the doctor or pharmacist if you are uncertain about your dose or about how to use this medicine.
Treatment with **Recormon** must be started under the medical supervision of your doctor.

The rest of the treatment is given by your doctor or, after receiving proper training, you can self-inject **Recormon** under the skin. The injection instructions are provided later on in this leaflet.

Recormon can be injected under the skin in the abdomen, arm or thigh; or into a vein. Your doctor will decide which option is best for you.

Usual dosage
The dosage and treatment regimen will be determined by the doctor only.
The **Recormon** dosage depends on the condition of your disease, the mode of administration (subcutaneous or intravenous injection) and on your body weight. Your doctor will determine the dosage suitable for you.
The doctor will use the lowest effective dosage to control the symptoms of your anemia.
If you do not respond adequately to **Recormon**, the doctor will check your dosage and will inform you if you need to change the **Recormon** dosage.
Do not exceed the recommended dose.

If you accidentally took a higher dosage, do not increase the dosage your doctor has prescribed for you. If you think you injected a dosage higher than you should have, refer to your doctor. It is unlikely that this will have a serious effect. No signs of poisoning, even with very high levels in the blood, have been observed. If you took an overdose, or if a child has accidentally swallowed the medicine, immediately refer to a doctor or proceed to a hospital emergency room and bring the package of the medicine with you.

If you forgot to take the medicine at the scheduled time, or if you injected too little, refer to your doctor. Do not take a double dose to compensate for a forgotten dose.
Adhere to the treatment regimen as recommended by the doctor.
Even if there is an improvement in your health condition, do not stop treatment with the medicine without consulting with the doctor.

How can you contribute to the treatment success?
Recormon is a pre-filled syringe intended for single use!
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 further questions regarding use of the medicine, consult the doctor or pharmacist.

4) SIDE EFFECTS

As with any medicine, the use of **Recormon** 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.

Refer to a doctor immediately if the following symptoms occur:

For all patients:
- A very rare side effect (affects up to 1 in 10,000 users) - severe allergic reaction, especially after the injection, manifested by wheezing or breathing difficulties; swelling of the tongue, face, throat, or swelling around the injection site; feeling dizzy, fainting or collapsing.
- Serious skin rashes including Stevens-Johnson syndrome (SJS) and toxic epidermal necrolysis (TEN) have been reported in association with epoetin treatment. These can appear as reddish lesions (target-board-like lesions) or circular patches, often with central blisters on the body. Also, skin peeling, ulcers of the mouth, throat, nose, genitals and eyes can occur, and may be preceded by fever and flu-like symptoms.
  Stop taking **Recormon** if you develop these symptoms and contact your doctor or seek medical attention immediately (see section 2).

In patients with chronic kidney disease (renal anemia):
- Headache, especially sudden, stabbing, migraine-like headache; confusion, speech disturbances, unsteady walking, fits or convulsions. These side effects may be a sign of a sharp increase in blood pressure (hypertensive crisis), even if your blood pressure is usually normal or low. Treat this immediately.
- Lack of energy and unusual fatigue can be signs of development of antibodies to erythropoietin (Pure Red Cell Aplasia - PRCA) (rare). PRCA means that the body has stopped or reduced the production of red blood cells. This causes severe anemia, manifested by symptoms that include unusual fatigue and lack of energy. If you developed antibodies to erythropoietin, the doctor will discontinue treatment with **Recormon** and will prescribe an alternative treatment for anemia.

Additional side effects that can affect any patient:
- Very common side effects (affect more than 1 in 10 users) - decreased blood iron levels may occur. Almost all patients need to take iron supplements during the course of treatment with **Recormon**.
- Rare side effects (affect up to 1 in 1,000 users) - allergies or skin reactions, such as rash or hives, itching or a reaction around the injection site.
- Very rare side effects (affect up to 1 in 10,000 users) - flu-like symptoms, especially at the beginning of treatment. These symptoms include fever, chills, headaches, pain in the limbs, pain in the bones, and/or feeling generally unwell. These reactions are usually mild to moderate and pass within a few hours or days.

Additional side effects in patients with chronic kidney disease (renal anemia):
- Very common side effects (affect more than 1 in 10 users) - increase in blood pressure, worsening of existing high blood pressure and headaches. The attending doctor will regularly check your blood pressure, particularly at the beginning of treatment. The doctor may treat the high blood pressure with appropriate medicines or by temporary interruption of **Recormon**.
- If you have low blood pressure or shunt (a vessel that enables connection to the dialysis system) complications, you may be at risk of developing shunt thrombosis (a blood clot in the vessel used for connection to the dialysis system).
- Very rare side effects (affect up to 1 in 10,000 users) - high blood potassium or phosphate levels. This condition can be treated by the doctor.

Additional side effects in adults receiving chemotherapy for cancer:
- Increase in blood pressure and headache can occasionally occur. Your doctor can treat high blood pressure with appropriate medicines.
- An increase in the formation of blood clots has been observed.

Additional side effects in patients due to donation of blood to themselves before surgery:
- A slight increase in the formation of blood clots has been observed.

If a side effect occurs, if any of the side effects worsens or if you suffer from a side effect not mentioned in this leaflet, consult with the doctor.
Side effects can be reported to the Ministry of Health by clicking on the link "Report Side Effects of 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 SHOULD THE MEDICINE BE STORED?

- Avoid poisoning! This medicine and any other medicine must be kept in a safe 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 this medicine in the refrigerator, at a temperature between 2-8°C.
- For the patient's information: The **Recormon** syringe can be taken out of the refrigerator and left at room temperature (not above 25ºC) for a single period of up to 3 days. Do not use **Recormon** that has been exposed to room temperature for more than 3 days.
- Keep the syringes in the original package in order to protect from light.
- Do not discard the medicine via household waste or wastewater. Ask the pharmacist how to dispose of the medicine in order to protect the environment.

6) FURTHER INFORMATION

In addition to the active ingredient, the medicine also contains:
Water for injection, glycine, disodium hydrogen phosphate, L-leucine, L-isoleucine, calcium chloride, sodium dihydrogen phosphate, sodium chloride, L-threonine, L-glutamic acid, L-phenylalanine, polysorbate 20, urea.

What the medicine looks like and contents of the package:
Recormon is a clear, colorless solution provided in a pre-filled syringe, in packages of 1, 4 or 6 syringes, depending on the dosage.
Not all package sizes may be marketed.

License holder and address: Roche Pharmaceuticals (Israel) Ltd., P.O.B. 6391, Hod Hasharon 4524079.
Manufacturer and address:
Roche Diagnostics GmbH, Germany - Sandhofer Strasse 116, Mannheim, Germany.

This leaflet was revised in January 2022 according to MOH guidelines.
Registration number of the medicine in the National Drug Registry of the Ministry of Health:
Recormon 4,000 IU/0.3 ml pre-filled syringe 121.08.30142
Recormon 5,000 IU/0.3 ml pre-filled syringe 114.42.29586
Recormon 6,000 IU/0.3 ml pre-filled syringe 121.40.30195
Recormon 10,000 IU/0.6 ml pre-filled syringe 114.43.29587
Recormon 30,000 IU/0.6 ml pre-filled syringe 132.41.31158

7) INSTRUCTIONS FOR SELF-INJECTION OF RECORMON PRE-FILLED SYRINGE:

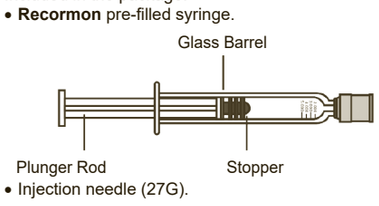
The following instructions for injection explain how to give an injection of **Recormon**. Be sure that you read, understand and follow the instructions below before injecting the medicine. Your doctor will show you how to prepare and inject the medicine properly before you use it yourself for the first time. Do not inject yourself unless you have received training. Consult your doctor if you require further information.

Recormon can be administered through two routes, your doctor will decide which way is right for you:
- Intravenous administration (into the vein), only to be performed by healthcare professionals.
- Subcutaneous administration (under the skin).

Before the injection:
- **Do not** take the needle cap off until you are ready to inject **Recormon**.
- **Do not** try to take the syringe apart at any time.
- **Do not** reuse the same syringe.
- **Do not** use if the syringe has been dropped or damaged.
- **Do not** leave the syringe unattended.
- Keep the syringe, the needle and the sharps disposal container out of reach of children.
- Contact your healthcare professional if you have any questions.

Storage Instructions:
- Keep your unused syringe(s) in the original carton and store in a refrigerator at 2˚C to 8˚C.
- Keep your syringe out of direct sunlight.
- **Do not** freeze the syringe.
- **Do not** use if the syringe has been frozen.
- Always keep the syringe dry.

Supplies needed to give your injection:
Included in the package:
- **Recormon** pre-filled syringe.



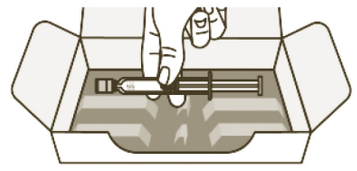
- Injection needle (27G).

Note: Each package contains 1 syringe/1 needle, 4 syringes/4 needles or 6 syringes/6 needles, depends on the dosage.
Not all package sizes may be marketed.

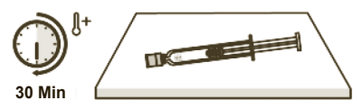
- Patient Leaflet

Not included in the package:
- alcohol swab
- sterile pad
- sharps container for safe disposal of needle and used syringe

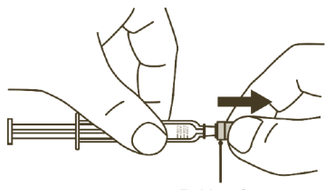
Preparing for injection
1. Find a well-lighted, clean, flat, working surface. Take the carton package with the syringe and needle out of the refrigerator.
2. Check the package has not been damaged and check the expiration date on the package has not passed. Do not use the medicine if the expiration date has passed, if the syringe is dropped or damaged, or if the carton package appears to be tampered with. In this case, proceed to step 17 and contact your attending healthcare provider.
3. Take one syringe out of the carton and one needle from the needle box. Be careful when taking out the syringe. Make sure you always hold the syringe as shown in the picture below.
   - **Do not** flip the package upside down to remove the syringe.
   - **Do not** handle the syringe by holding the plunger or needle cap.
   - If syringes remain in the package, put the carton with the remaining syringes and needles back into the refrigerator.



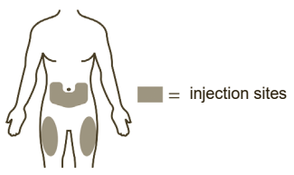
4. Inspect the syringe and needle closely.
   - Check the syringe and needle for any damage. **Do not** use the syringe if you have dropped the syringe or if any part of the syringe appears to be damaged.
   - Check the expiration date on the syringe and the needle. **Do not** use the syringe or the needle if the expiration date has passed.
   - Check the liquid in the syringe. The solution should be clear and colorless. **Do not** use the syringe if the solution is cloudy, discolored, or has particles.
5. Place the syringe on a clean, flat surface.
   - Set aside the syringe for 30 minutes so it can warm up on its own to room temperature. Leave the needle cap on while the syringe warms up.
   - **Do not** speed up the warming process in any way, and **do not** put the syringe in a microwave or in warm water.
   - If the syringe does not reach room temperature, this could cause the injection to feel uncomfortable and make it hard to push the plunger.



6. Attach the needle to the syringe.
   - Remove the needle from its package.
   - Pull the rubber cap off the end of the syringe.
   - Dispose of the rubber cap in a sharps container immediately.
   - **Do not** touch the tip of the syringe.
   - **Do not** push or pull the plunger.
   - Hold the syringe by the barrel and push the needle onto the syringe.
   - Gently twist the needle until it is fully attached.

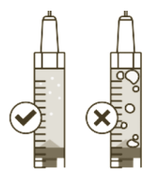


7. Place the syringe on a clean, flat surface until ready for use.
8. Wash your hands with soap and water.
9. Choose an injection site:
   - The recommended injection sites are the top part of your thigh or the lower part of your abdomen (below the belly button). **Do not** inject within 5 centimeters of your belly button.
   - Choose a different injection site for each new injection.
   - **Do not** inject the medicine into moles, scars, bruises, or areas where the skin is tender, red, hard or damaged.
   - **Do not** inject the medicine into a vein or into a muscle.



10. Wipe the injection site with an alcohol swab and let it air dry for 10 seconds.
    - **Do not** fan or blow on the cleaned area.
    - **Do not** touch the wiped injection site again before giving the injection.

Subcutaneous Injection
11. Hold the syringe and needle tightly at the hub and carefully pull the injection needle cap away from the syringe. Use the syringe within five minutes of removing the cap; otherwise, the needle may clog.
    - **Do not** hold the plunger while you remove the needle cap.
    - **Do not** touch the needle after removing the needle cap.
    - **Do not** try to re-cap the needle.
    - Throw away the needle cap in a sharps container immediately.
12. Hold the syringe with the needle pointing up. Remove the large air bubbles by gently tapping the syringe barrel with your fingers until the air bubbles rise to the top of the syringe. Then, slowly push the plunger up to push the air bubbles out of the syringe.



13. Adjust to your prescribed dose by slowly pushing the plunger.
14. Pinch the skin at the selected injection site and fully insert the needle at a 45° to 90° angle with a quick, firm action.
    - **Do not** touch the plunger while inserting the needle into the skin
    - **Do not** insert the needle through clothing.
    - Once the needle is inserted, release the pinch and hold the syringe in place.
15. Slowly inject your prescribed dose by gently pushing the plunger downward.
    - Remove the needle and syringe from the injection site at the same angle as inserted.

After the injection
16. There may be a little bleeding at the injection site. You can press a dry sterile pad over the injection site. **Do not** rub the injection site.
    - If needed, you may cover the injection site with a small bandage.
    - In case of skin contact with medicine, wash the area that touched the medicine with water.
17. Put your used syringe in a sharps disposal container right away after use.
    - **Do not** try to remove the used injection needle from the used syringe.
    - **Do not** try to recap the injection needle with the cap.
    - **Do not** throw away (dispose of) the syringe in your household trash.
    - Always keep the sharps disposal container out of reach of children.