Roferon_PL_Ver 2

This leaflet was checked and approved by the Ministry of Health in May 2016 and was updated in accordance with the Ministry of Health guidelines in June 2018.

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

The medicine is dispensed with a doctor's prescription only

Roferon-A® 3 million IU/0.5 ml Pre-filled syringe

Composition:
Each syringe contains: Interferon alfa-2a 3 MIU

Roferon-A® 4.5 million IU/0.5 ml Pre-filled syringe

Composition:
Each syringe contains: Interferon alfa-2a 4.5 MIU

The active ingredient in each syringe - interferon alfa-2a.
* For information regarding the inactive ingredients, see 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.
This medicine has been prescribed for the treatment of 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.

Important information for your review
- Consult the doctor before using the medicine if you are planning to become pregnant, if you are pregnant or if you are breast-feeding. For information regarding pregnancy and breast-feeding in women treated with the medicine and in the partners of men treated with the medicine, read section 2, subsection - "Pregnancy, fertility and breast-feeding".
- **Roferon-A** can be injected by a doctor or nurse or self-injected. If you self-inject the preparation, be sure that you have received appropriate training. See section 7 - "Instructions for self-injecting **Roferon-A**".
- The preparation is intended for single use!
- Store the medicine in the refrigerator; do not freeze. Keep the syringe in the original carton package.

1) WHAT IS THE MEDICINE INTENDED FOR?

The medicine is intended for treatment of the following indications:
- Chronic type B or C viral infection of the liver
- Certain types of blood cancer (hairy cell leukaemia, chronic myelogenous leukaemia [CML])
- Other forms of cancer (renal cell carcinoma, AIDS-related Kaposi's sarcoma, follicular non-Hodgkin's lymphoma and malignant melanoma)
- Warts in the genital area (*Condylomata acuminata* type)

If you are not sure why **Roferon-A** has been prescribed for you, you should discuss your illness and its treatment with the attending doctor.

Therapeutic group: interferons

Roferon-A contains an antiviral agent called interferon alfa-2a which is similar to the natural substance produced by the body to protect against viral infections, tumors and against foreign substances that may invade the body. Once **Roferon-A** detects and attacks a foreign substance, it alters it by slowing, blocking, or changing its activity or ability to proliferate.

2) BEFORE USING THE MEDICINE

Do not use the medicine if:
- You are sensitive (allergic) to the active ingredient, interferon alfa-2a, or to any of the additional ingredients contained in the medicine (for the list of inactive ingredients, see section 6 - "Further Information").
- You suffer or have suffered in the past from heart disease.
- You have severe impairment of kidney or liver function.
- You have a bone marrow disorder.
- You suffer from seizures, e.g., epilepsy and/or other central nervous system disorders.
- You have a liver disease or liver cirrhosis.
- You are being treated, or have recently been treated, with medication for a chronic liver disease that weakens your immune response.
- **Roferon-A is not recommended for use in children.** "Gasping syndrome" (a serious condition in children up to age 3), is associated with administration of benzyl alcohol, which is an inactive ingredient in **Roferon-A**. **Roferon-A** is therefore not suitable for use in children (including premature babies, newborns or infants). For further information, see section 2, subsection - "Important information regarding some of the ingredients of the medicine **Roferon-A**".
- For certain diseases, **Roferon-A** can be used in combination with other medicines. In these cases, additional restrictions regarding the use of **Roferon-A** will be explained to you by the doctor.

Special warnings regarding use of the medicine
Consult with the doctor or pharmacist before using **Roferon-A**.

Before treatment with Roferon-A, tell the doctor if:
- You are pregnant or may be pregnant.
- You have mental disorders (psychiatric difficulties) or have had a mental (psychiatric) disorder in the past.
- You have psoriasis, a disease of recurring scaly lesions and dryness of the skin.
- You have kidney, liver or heart function problems.
- You have ever had an autoimmune disease, e.g., thyroid problems or inflammation of the blood vessels (vasculitis).
- You underwent an organ transplant (e.g., kidney) or bone marrow transplant in the past, or if you are a candidate to undergo an organ or bone marrow transplant in the near future.
- You have a low blood cell count.
- You have problems relating to the blood system or diabetes (a disease resulting from high blood sugar levels). The doctor may ask you to have periodic blood tests performed during the course of treatment, in order to check the blood composition, since changes in the blood composition may occur during the course of treatment with the medicine. When necessary, the attending doctor will adjust for you the dosage of **Roferon-A** and of other medicines you are taking concomitantly.
- You are being treated for chronic hepatitis C.
- You are an HIV (human immunodeficiency virus) carrier being treated with anti-HIV medicines.
- You are taking any other medicines (including medicines not prescribed by your doctor).
- You are an adult and have, or have had in the past, a substance abuse (e.g., addiction to alcohol or to drugs).

Roferon-A and other medicines
If you are taking, or have recently taken or might take other medicines, including non-prescription medicines or nutritional supplements, tell the doctor or pharmacist.
The effect of other medicines given with interferons (e.g., **Roferon-A**) can get stronger, weaker or change. In particular, inform the doctor or pharmacist if you are taking theophylline, a medicine used to treat asthma. When this medicine is given together with interferon, its effect can increase and there may be a need to adjust the dosage.

Patients with an HIV infection:
Lactic acidosis and worsening of liver function are side effects associated with Highly Active Anti-Retroviral Therapy (HAART), a type of HIV treatment. If you are being treated with HAART, adding **Roferon-A** and ribavirin may increase your risk of lactic acidosis and liver failure. The attending doctor will monitor for signs and symptoms of these conditions. Also carefully read the ribavirin patient leaflet.

Blood tests
If you are going to have a blood test during the course of treatment with **Roferon-A**, tell the attending staff that you are taking **Roferon-A**. In uncommon or rare cases, **Roferon-A** may affect the results of blood tests.

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

Pregnancy, fertility and breast-feeding
Pregnancy and fertility
Do not use **Roferon-A** if you are pregnant, think you are pregnant, or are planning to become pregnant, unless your doctor recommends it. This is because **Roferon-A** may affect your baby. It is very important that you and your partner use effective contraception while you are being treated with **Roferon-A**.

When using **Roferon-A** in combination with ribavirin, if there is a chance of becoming pregnant, both male and female patients must take precautionary measures to prevent pregnancy, as ribavirin can cause significant harm to a fetus:
- If you are **a woman** of childbearing age who is taking **Roferon-A** in combination with ribavirin, you must present a negative pregnancy test before starting treatment, once a month during therapy and for 4 months after discontinuation of treatment. You and your partner must each use an effective contraceptive to prevent pregnancy for as long as you are taking the treatment and for 4 months after stopping treatment. This issue can be discussed with the attending doctor.
- If you are **a man** who is taking **Roferon-A** in combination with ribavirin, do not have sex with a pregnant woman unless you use a condom. This will lessen the chance of ribavirin being left in the woman's body. If your female partner is not pregnant now but is of childbearing age, she must perform a pregnancy test once a month during treatment and for 7 months after discontinuation of treatment. You and your partner must each use an effective contraceptive to prevent pregnancy for as long as you are taking the treatment and for 7 months after stopping treatment. This issue can be discussed with the attending doctor.

Breast-feeding
If you are breast-feeding, consult the doctor or pharmacist before taking medicines.
It is unknown whether this medicine is secreted into breast milk. Therefore, consult your attending doctor whether you should discontinue breast-feeding or discontinue **Roferon-A** treatment. In combination therapy of **Roferon-A** with ribavirin, please also read the ribavirin patient leaflet.

Driving and using machines
Do not drive or operate machinery if you feel dizzy, tired or confused during the course of treatment with **Roferon-A**.

Important information regarding some of the ingredients of the medicine Roferon-A
The medicine **Roferon-A** contains benzyl alcohol, and therefore it must not be given to premature babies or newborns and infants. This substance may cause "gasping syndrome", a dangerous syndrome that can cause toxic or allergic reactions in infants and children up to 3 years old.
This medicine contains less than 23 mg sodium per 0.5 ml, that is: the medicine is essentially 'sodium-free'.

3) HOW SHOULD YOU USE THE MEDICINE?

Always use according to the doctor's instructions.
Roferon-A can be injected by a doctor or nurse or self-injected. Do not attempt to self-inject **Roferon-A** without appropriate training by the nurse or the attending doctor. You should check with the doctor or pharmacist if you are uncertain.

Roferon-A, pre-filled syringe, is intended for subcutaneous (beneath the skin) injection. For detailed injection instructions, please see section 7 - "Instructions for self-injecting **Roferon-A**" further on in this leaflet.
The syringe is intended for single use.

The dosage and treatment regimen will be determined by the attending doctor only
The doctor will adjust the desired dose for you, in accordance with the disease you are suffering from and the side effects of the treatment.
Usually, the daily dosage will not exceed 36 million IU (MIU).
If you think the effect of the medicine is too weak or too strong, talk to the doctor. **Do not change the dosage before talking to your doctor. Do not exceed the recommended dose.**

If you accidentally took too high a dose, or if a child has accidentally swallowed the medicine, refer immediately to a doctor or proceed to a hospital emergency room, and bring the package of the medicine with you.

If you forget to take this medicine at the required time, do not take a double dose to compensate for the forgotten dose.

Adhere to the treatment as recommended by the attending doctor. Even if there is an improvement in your health, do not stop treatment with the medicine without consulting the doctor.

If you stop taking the medicine, refer to the attending doctor or pharmacist as soon as possible.

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

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

4) SIDE EFFECTS

As with any medicine, use of **Roferon-A** 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 the doctor immediately if you notice any of the following serious side effects. You may need urgent medical treatment:
- Development of signs of a severe allergic reaction (such as difficulty in breathing, wheezing or hives) while being treated with the medicine **Roferon-A**.
- Decreased vision during or after discontinuing treatment with the medicine **Roferon-A**.
- Development of signs of depression (such as: sadness, feeling lack of self-esteem or suicidal thoughts) during the course of treatment with **Roferon-A**.

Additional side effects:
Flu-like symptoms such as: tiredness, chills, muscle or joint pain, headache, sweating and fever are very common. These symptoms can be relieved by taking paracetamol. Your doctor will advise you regarding the dosage you should take. These symptoms usually lessen with continued therapy.

Very common side effects (effects that occur in more than one in ten users):
- low white blood cell counts (the signs include an increase in the number of infections)
- loss of appetite
- nausea
- low blood calcium levels
- diarrhea
- decreased appetite
- hair thinning or hair loss (these effects are usually reversible on completion of treatment)
- flu-like illness (symptoms can include tiredness, fever and chills)
- headache
- increased sweating
- muscle pain
- joint pain

Common side effects (effects that occur in 1-10 in 100 users):
- low number of red blood cells or anemia (the signs include feeling tired, pale skin and shortness of breath)
- low number of platelets (the signs include small bruises on the body or bleeding)
- changes in platelet and red blood cell counts are more likely to occur if you are undergoing cancer treatments, including chemotherapy, or have decreased bone marrow activity. Your blood cell count values will usually become more normal after discontinuing treatment with **Roferon-A**.
- irregular heartbeat
- palpitations
- bluish discoloration of the skin or lips (caused by a lack of oxygen in the blood)
- vomiting or feeling sick
- abdominal pain
- dry mouth
- bitter taste or change in the sensation of taste
- chest pain
- swelling
- weight loss

Uncommon side effects (effects that occur in 1-10 in 1,000 users):
- dehydration and electrolyte imbalance (abnormal blood test results for sodium or potassium)
- depression
- anxiety
- confusion
- changes in behavior or abnormal behavior
- nervousness
- forgetfulness
- sleep disturbances
- muscle weakness
- changes in sensation on the skin (for example, tingling of the skin, prickling, numbness)
- dizziness
- trembling of hands
- drowsiness or sleepiness
- conjunctivitis or redness of eyes
- visual disturbances
- temporary low or high blood pressure
- itching
- psoriasis or worsening of psoriasis
- urine tests may show protein and increased cell counts in the urine
- changes in liver function, shown in blood tests

Rare side effects (effects that occur in 1-10 in 10,000 users):
- pneumonia
- cold sores (herpes)
- genital herpes
- severe decrease in the number of white blood cells (agranulocytosis)
- abnormal breakdown of red blood cells (hemolytic anemia)
- autoimmune diseases (where the immune system mistakenly attacks the cells of the body)
- hypersensitivity reaction including: wheals (swelling of the skin, usually accompanied by itching), swelling of the face, lips and throat, wheezing and signs of an allergic reaction
- increased or decreased thyroid function
- high blood sugar levels or diabetes (a disease resulting from high blood sugar levels)
- thoughts of harming yourself, suicidal thoughts or suicide
- coma
- stroke
- convulsions
- transient or temporary impotence
- visual disturbances due to poor blood flow to the back of the eye (ischemic retinopathy)
- heart attack
- heart failure
- serious heart and breathing problems
- build-up of fluid in the lungs (may cause breathing difficulties)
- inflammation of the blood vessels (vasculitis)
- shortness of breath
- cough
- inflammation of the pancreas (pancreatitis)
- overactivity of the bowels (may cause diarrhea)
- constipation
- heartburn
- flatulence
- the liver may work less well than usual, and even severe liver disorders may occur, including liver failure or inflammation of the liver (hepatitis)
- rash
- dry skin, lips or mouth
- nosebleed
- dry or runny nose
- autoimmune disease (where the immune system mistakenly attacks parts of the body), which often causes rash and joint pain and may even affect other parts of the body (your doctor may call the disease lupus or systemic lupus erythematosus)
- arthritis or joint pain
- kidney failure or worsening of kidney function (may mainly occur in cancer patients with a pre-existing kidney disease)
- changes in kidney function shown in blood tests
- changes in uric acid and lactate dehydrogenase levels, shown in blood tests
- mania (episodes of exaggerated elevation of mood)

Very rare side effects (effects that occur in less than one in 10,000 users):
- an autoimmune disease where the immune system mistakenly attacks the platelets (cells responsible for blood clotting) and it can therefore cause a severe decrease in the number of platelets, manifested by development of small bruises, which look like spots on the skin
- sarcoidosis (a disease that results from inflammation of tissues of the body). Sarcoidosis can harm almost any part of the body, but most often starts in the lungs or lymph nodes
- hypertriglyceridemia and hyperlipidemia (high levels of certain fats in the blood)
- damage to the retina (the back part of the eye) or to the blood vessels within the retina, which can cause blurred vision or, in severe cases, to loss of eyesight
- on examination of the eyes, the doctor may notice changes in the retina, including swelling of the main nerve at the back part of the eye
- visual disturbances related to the main nerve at the back part of the eye
- worsening or recurrence of a peptic ulcer and intestinal bleeding
- redness, swelling and pain of the skin around the injection site of **Roferon-A**; and a dead patch of skin around the injection site can appear
- disorders related to mental state, such as difficulty with thinking, concentration, personality changes or level of consciousness (your doctor may call the disease encephalopathy)

Side effects of unknown frequency (effects whose frequency has not been determined):
- Organ transplant rejection.
- Ischemic colitis (insufficient blood supply to the bowels) and ulcerative colitis. Abdominal pain, bloody diarrhea and fever are typical signs of colitis.
- Pulmonary arterial hypertension - a disease in which there is severe narrowing of the blood vessels in the lungs, resulting in high blood pressure in the blood vessels that carry blood from the heart to the lungs. This disease may occur in particular in patients with risk factors, such as: HIV infection or severe liver problems (cirrhosis). This disease may develop at various time points during the course of treatment, typically several months after starting treatment with **Roferon-A**.
- Ear disorders: hearing loss
- Skin disorders: skin discoloration

The doctor can decide to combine **Roferon-A** with other medicines. In such a case, you may experience additional side effects. You can discuss this with your attending doctor.

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

Reporting of side effects:
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://forms.gov.il/globaldata/getsequence/getsequence.aspx?formType=AdversEffectMedic@moh.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 of children and/or infants in order to avoid poisoning. Do not induce vomiting unless explicitly instructed to do so by the doctor.
- Even with recommended packaging/storage conditions, medicines retain their potency for a limited period of time only. Please note the expiry date of the preparation. Do not use the medicine after the expiry date (exp. date) that appears on the package and syringe. The expiry date refers to the last day of that month. In any case of doubt, consult the pharmacist who dispensed the medicine to you.
- Store in a refrigerator (2°C-8°C; this temperature range prevails in most household refrigerators). Do not freeze. Keep the syringe in its original carton package to protect it from light. Do not store different medications in the same package.
- Do not use the medicine if the solution is cloudy, if there are particles floating in the solution or if the color of the solution is not transparent to slightly yellowish.
- The preparation is intended for single use!
- Do not discard the medicine via the wastewater or to household waste bin. Consult the pharmacist on how to dispose of medicines no longer in use. These measures will help protect the environment.

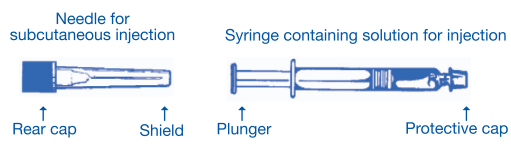
6) FURTHER INFORMATION

The active ingredient is interferon alfa-2a, and the medicine is available in strengths of 3 million IU/0.5 ml and 4.5 million IU/0.5 ml.
In addition to the active ingredient, the medicine also contains:
Benzyl alcohol, sodium chloride, ammonium acetate, polysorbate 80, glacial acetic acid, sodium hydroxide, water for injection.

What the medicine looks like and what are the contents of the package?
The medicine **Roferon-A** is marketed as a solution for injection (in a pre-filled syringe containing 0.5 ml). Each package contains one syringe.
The solution is clear, transparent to slightly yellowish.
License holder and address: Roche Pharmaceuticals (Israel) Ltd., P.O.B. 6391, Hod Hasharon 4524079.
www.roche.co.il
Manufacturer name and address: F. Hoffmann-La Roche Ltd., Basel, Switzerland.
The format of this leaflet was determined by the Ministry of Health and its content was checked and approved in May 2016 and was updated in accordance with the Ministry of Health guidelines in June 2018.
Registration number of the medicine in the National Drug Registry of the Ministry of Health:
Roferon-A 3 million IU/0.5 ml, pre-filled syringe: 108.53.29258.00.
Roferon-A 4.5 million IU/0.5 ml, pre-filled syringe: 108.54.29259.00.

7) INSTRUCTIONS FOR SELF-INJECTING ROFERON-A

Instructions for subcutaneous (beneath the skin) injection of **Roferon-A** pre-filled syringe.



Important: Allow the solution to reach room temperature before injecting.

1. Take the needle out of the package. Pull off the cap found at the back end of the needle. Then, take the syringe out of the package and take off the protective cap of the syringe. Tightly connect the needle to the syringe. Pull off the protective shield of the needle (see Figure no. 1).

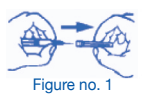


Figure no. 1

2. Hold the syringe, with the needle pointing upward. Carefully push out any air by slowly pushing the plunger into the syringe.


Figure no. 2

3. The medicine **Roferon-A** can be injected either into the thigh or into the lower abdomen. It is recommended to choose a different injection site each time.

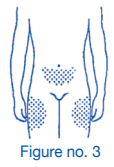


Figure no. 3

4. Before self-injecting, clean the injection site with an alcohol swab.

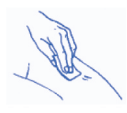


Figure no. 4

5. Use your thumb and index finger to pinch and form a fold of skin at the injection site. Insert the needle as far as it will go at a 45-degree angle (see Figure no. 5). Pull back the plunger of the syringe slightly.
If blood appears in the syringe, it is a sign that the needle has been inserted into a blood vessel. In this case, do not inject the substance. Discard the unused syringe and needle and start again at a different injection site with a new syringe and needle.


Figure no. 5

6. Applying steady pressure, inject the contents of the syringe beneath the skin until the syringe is completely empty.

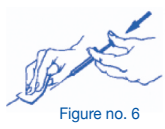


Figure no. 6

7. To remove the syringe, press the alcohol swab gently on the injection site and withdraw the needle at a lower angle.


Figure no. 7

The pre-filled syringes are intended for single use only. Discard any remaining substance. Ask the doctor or pharmacist if you are uncertain.

Adhere to the following points regarding the use and disposal of syringes and other medicinal sharps:
- Do not reuse syringes and needles.
- Discard all the syringes and needles into a designated container (a puncture-proof container).
- Keep the container out of the reach of children.
- Do not discard the used container into the household waste bin.
- Dispose of the container according to the doctor's or nurse's instructions.