Genisys-No.	10158447
Printing Colour:	Pantone Black
Format:	148x840 mm
Folding Format:	148x210 mm
Type Size	11 pt
Drawing Norm	NP9345 11.08.10 97.4.3525
make-up code	GB

Checked and approved	Date	Signature

Good To Print	Version	Date	Signature
MMBFMM8W			
MMBFMM8Z	3	27.02.15	

Package Leaflet: Information for the user

Roferon®-A

3 million international units (IU)
4.5 million international units (IU)
6 million international units (IU)
9 million international units (IU)
solution for injection in pre-filled syringe

Interferon alfa-2a

Read all of this leaflet carefully before you start using this medicine because it contains important information for you.
- Keep this leaflet. You may need to read it again.
- If you have any further questions, ask your doctor or pharmacist.
- This medicine has been prescribed for you only. Do not pass it on to others. It may harm them, even if their signs of illness are the same as yours.
- If you get any side effects, talk to your doctor or pharmacist. This includes any possible side effects not listed in this leaflet. See section 4.

What is in this leaflet:

1. What Roferon-A is and what it is used for

Roferon-A contains an antiviral agent called interferon alfa-2a which is similar to a natural substance produced by the body to protect against viral infections, tumors and foreign substances that may invade the body. Once Roferon-A has detected and attacked a foreign substance, it alters it by slowing, blocking, or changing its growth or function.

Roferon-A is used to treat the following:
- Viral infections, such as chronic hepatitis B and C.
- Cancers of the blood (cutaneous T-cell lymphoma, hairy cell leukaemia and chronic myelogenous leukaemia).
- Some other forms of cancer (renal cell carcinoma, AIDS-related Kaposi's sarcoma, follicular non-Hodgkin's lymphoma and malignant melanoma).

If you are not sure why you have been prescribed Roferon-A, you should discuss your illness and its treatment with your doctor.

2. What you need to know before you use Roferon-A

Do not use Roferon-A:
- if you are allergic to interferon alfa-2a or any of the other ingredients of this medicine (listed in Section 6).
- if you suffer or have suffered from heart disease.
- if you have a severe kidney or liver condition.
- if you have a bone marrow disorder.
- if you suffer from seizures e.g. epilepsy and/or other central nervous system disorders.
- if you have a liver disease or liver cirrhosis
- if you are or have recently been treated with medication for chronic liver disease that weakens your immune response.

Roferon-A is not recommended for use in children except on the advice of your doctor. 'Gasping syndrome' (a serious condition in children up to 3 years old), has been linked with benzyl alcohol. Benzyl alcohol is an inactive ingredient in Roferon-A. Roferon-A is therefore not a suitable medicine for young children (including premature babies, newborns or infants).

For some diseases, Roferon-A may be used in combination with other drugs. In such cases any additional restrictions on the use of Roferon-A will be explained to you by your doctor.

Warnings and precautions
Talk to your doctor or pharmacist before using Roferon-A.
Tell your doctor:
- if you have mental problems (psychiatric difficulties) or have ever had a mental (psychiatric) illness.
- if you have psoriasis (a disease of recurring dry, patchy, scaly skin lesions).
- if you have kidney, heart or liver problems.
- if you have ever had an autoimmune disease, e.g. thyroid problems, vasculitis (inflammation of the blood vessels).
- if you have had an organ transplant (such as kidney) or bone marrow transplant, or have one planned in the near future.
- if you are or may be pregnant.
- if you have a low blood cell count.
- if you have diabetes (a disease resulting from high sugar level in your blood).
- if you have any other problems with your blood.
- if you are being treated for chronic hepatitis C.
- if you are also infected with HIV and being treated with anti-HIV medicines.
- if you are taking any other medicines (including those not prescribed by your doctor).
- if you are an adult who has or had a history of substance abuse (e.g. alcohol or drugs)

Tell your doctor if you have a blood disorder or suffer from diabetes. Your doctor may take samples of your blood at intervals to check its composition, which may change during treatment. If needed your doctor may adjust the dose of your treatment with Roferon-A and any other treatments you are receiving at the same time.

Other medicines and Roferon-A
Tell your doctor or pharmacist if you are taking, have recently taken or might take any other medicines. The effects of those medicines could either be increased, decreased, or altered when administered at the same time as interferons. In particular the plasma concentration of theophylline, an asthma medicine from the xanthine family, can be increased when it is administered at the same time as interferon and may require a dosage adjustment.

Patients who also have HIV infection:
Lactic acidosis and worsening liver function are side effects associated with Highly Active Anti-Retroviral Therapy (HAART), an HIV treatment.

If you are receiving HAART, the addition of Roferon-A and Ribavirin may increase your risk of lactic acidosis or liver failure. Your doctor will monitor you for signs and symptoms of these conditions. Please read the Ribavirin Package Leaflet.

Blood tests. If you are going to have a blood test, you should tell the doctor or nurse performing the test that you are taking Roferon-A. In some uncommon or rare cases, Roferon-A may affect the results of these tests.

Pregnancy and fertility
Do not use Roferon-A if you are pregnant, think you may be pregnant, or are planning to have a baby, unless your doctor tells you to. This is because Roferon-A may affect your baby. It is important that you and your partner use an effective method of birth control (contraception) while you are being treated with Roferon-A.

When Roferon-A is used in combination with ribavirin, both male and female patients must take special precautions in their sexual activity if there is any chance for pregnancy to occur as ribavirin can be very damaging to an unborn baby:
- if you are a **woman** of childbearing age who is taking Roferon-A in combination with ribavirin, you must have a negative pregnancy test before treatment, each month during therapy and for the 4 months after treatment is stopped. You and your partner must each use an effective contraceptive during the time you are taking the treatment and for 4 months after stopping treatment. This can be discussed with your doctor**.**
- if you are a **man** who is taking Roferon- A in combination with ribavirin, do not have sex with a pregnant women unless you use a condom. This will lessen the chance for ribavirin to be left in the woman's body. If your female partner is not pregnant now but is of childbearing age, she must be tested for pregnancy each month during treatment and for 7 months after treatment has stopped. You and your partner must each use an effective contraceptive during the time you are taking the treatment and for the 7 months after stopping treatment. This can be discussed with you doctor.

Breast-feeding
If you are breast-feeding, ask your doctor or pharmacist for advice before taking this medicine. It is not known whether this medicine is present in human milk. Therefore, discuss with your doctor whether you should suspend breast-feeding or discontinue Roferon-A. In combination therapy with ribavirin, take notice of the respective informing texts of ribavirin containing medicines.

Driving and using machines
Do not drive or use machinery if you feel drowsy, tired or confused while using Roferon-A.

Roferon-A contains benzyl alcohol
Roferon-A contains benzyl alcohol therefore it must not be given to premature babies or newborns. It may cause toxic or allergic reactions in infants and children up to 3 years old.

The medicine contains less than 1 mmol sodium (23 mg) per 0.5 ml, i.e. essentially "sodium free".

3. How to use Roferon-A

Always use this medicine exactly as your doctor has told you. Check with your doctor or pharmacist if you are not sure.

Roferon-A can be given by your doctor or nurse, or your doctor or nurse may teach you how to inject yourself with Roferon-A. Do not try to inject yourself with Roferon-A unless you have received training. You should check with your doctor or nurse if you are not sure.

Roferon-A pre-filled syringes are used to give an injection beneath your skin (subcutaneous). See section 7 for detailed instructions.

The pre-filled syringes are for single use only.

Roferon-A dosing
Your doctor will decide the best dose for you.
The amount of Roferon-A you need will depend on why you are being treated and the side effects you suffer.

Your dose should not normally be more than 36 million International Units (IU) per day.

If you think the effect of your medicine is too weak or too strong talk to your doctor. **Do not change the amount you take before talking to your doctor.**

The recommended dose is:

Hairy Cell Leukaemia
3 million IU daily for 16-24 weeks.

Chronic Myelogenous Leukaemia
The dose will normally be increased from 3 million IU to 9 million IU taken once a day over an initial treatment period of 12 weeks.

Cutaneous T-Cell Lymphoma
The dose will normally be increased from 3 million IU to 18 million IU taken once a day over an initial treatment period of 12 weeks.

AIDS-related Kaposi's Sarcoma
The dose will normally be increased from 3 million IU to 18 million IU taken once a day to a maximum of 36 million IU over an initial treatment period of 10-12 weeks.

Renal Cell Carcinoma
Combination with vinblastine
The dose will normally be increased from 3 million IU to 18 million IU taken three times a week over an initial treatment period of 12 weeks.
Combination with bevacizumab (Avastin)
9 million IU under the skin (subcutaneously) three times a week until your disease progresses or for up to 1 year.

Chronic Hepatitis B
2.5-5 million IU/square metre body surface area three times a week for 4-6 months.

Chronic Hepatitis C
3-6 million IU three times a week for 6-12 months.

Follicular Non-Hodgkin's Lymphoma (with chemotherapy)
6 million IU/square metre body surface area from day 22 to day 26 of each 28-day cycle

Malignant Melanoma
3 million IU three times a week for 18 months.

If you respond well to initial treatment with Roferon-A, your doctor may decide that you should continue treatment for a longer period of time (maintenance therapy) and will change your dosage accordingly.

Combination therapy with Ribavirin in chronic hepatitis C
When taking Roferon-A and Ribavirin at the same time, please follow the dosage regimen recommended by your doctor**.**

Your doctor will tell you when to stop using Roferon-A. Some illnesses may require treatment over a period of several years.

If you use more Roferon-A than you should
Contact your doctor, pharmacist or nearest hospital immediately.

If you forget to use Roferon-A
Do not take a double dose to make up for a forgotten dose.

If you stop using Roferon-A
Contact your doctor or pharmacist as soon as possible.
If you have any further questions on the use of this medicine, ask your doctor, pharmacist or nurse.

4. Possible side effects

Like all medicines, this medicine can cause side effects, although not everybody gets them.

Tell your doctor straight away if you notice any of the following serious side effects. You may need urgent medical treatment:
- If you develop signs of a severe allergic reaction (such as difficulty in breathing, wheezing or hives) while on this medication.
- If you notice a decrease in your sight during or after treatment with Roferon-A.
- If you develop any signs of depression (such as sadness, feeling worthless or thoughts of suicide) during your Roferon-A treatment.

Please turn over ➡

Genisys-No.	10158447
Printing Colour:	Pantone Black
Format:	148x840 mm
Folding Format:	148x210 mm
Type Size	11 pt
Drawing Norm	NP9345 11.08.10 97.4.3525
make-up code	GB

Checked and approved	Date	Signature

Good To Print	Version	Date	Signature
MMBFMM8W			
MMBFMM8Z	3	27.02.15	

Other possible side effects:

It is very common to experience flu-like symptoms such as tiredness, chills, muscle or joint pain, headache, sweating and fever. These effects can usually be reduced by taking paracetamol. Your doctor will advise you on the dose you should take. These kinds of symptoms usually lessen with continued therapy.

Other very common side effects (may affect more than 1 in 10 people) are:
- lower white cell counts. The signs include increased number of infections
- loss of appetite
- nausea
- low blood calcium
- diarrhoea
- decreased appetite
- hair thinning or hair loss (this is usually reversible on completion of treatment)
- flu-like illness. Symptoms may include tiredness, fever and chills
- headache
- increased sweating
- muscle pain
- joint pain

Common side effects (may affect up to 1 in 10 people):
- lower number of red blood cells or anaemia (the signs include feeling tired, pale skin and being short of breath)
- lower numbers 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. The make-up of your blood will usually become more normal after discontinuing Roferon-A.
- irregular heartbeat
- palpitations
- bluish discolouration of the skin or lips (caused by a lack of oxygen in the blood)
- vomiting or feeling sick
- stomach pains
- dry mouth
- bitter taste or change in the sensation of taste
- chest pain
- swelling
- weight loss

Uncommon side effects (may affect up to 1 in 100 people):
- dehydration and electrolyte imbalance (abnormal blood test results for sodium or potassium)
- depression
- anxiety
- confusion
- changed or abnormal behaviour
- nervousness
- forgetfulness
- sleep disturbances
- muscle weakness
- changes to sensation of the skin, e.g. pins and needles, numbness,
- dizziness
- trembling of hands
- drowsiness or sleepiness
- conjunctivitis or redness of eyes
- visual disturbances
- temporary low or high blood pressure
- itchiness
- psoriasis or worsening of psoriasis
- urine tests may show protein and increased cell counts in your urine
- blood tests: showing changes in liver function

Rare side effects (may affect up to 1 in 1000 people):
- pneumonia
- cold sores
- genital herpes
- severe decrease in the number of white blood cells (your doctor may call this agranulocytosis)
- abnormal breakdown of red blood cells (your doctor may call this haemolytic anaemia)
- autoimmune conditions (where your immune system attacks your cells by mistake),
- hypersensitivity reactions including wheals, swelling of the face, lips and throat, wheezing and allergic type reactions
- increased or decreased activity of the thyroid
- blood tests showing high blood sugar or diabetes (a disease resulting from high blood sugar)
- suicide or thinking about committing suicide or harming yourself
- coma
- stroke
- convulsions (fits)
- transient or temporary impotence (male sexual dysfunction)
- visual disturbance due to poor blood flow to the back of the eye (your doctor may call this ischaemic retinopathy)
- heart attack
- heart failure
- serious heart and breathing problems
- build-up of fluid in the lungs (which may cause breathing problems)
- inflammation of the blood vessels [vasculitis]
- breathlessness
- cough
- inflammation of the pancreas (your doctor may call this pancreatitis)
- over activity of the bowels (this may cause diarrhoea)
- constipation
- heartburn
- flatulence (wind)
- the liver may work less well than usual and may result in severe liver abnormalities, including liver failure or inflammation of the liver (also known as hepatitis)
- rash
- dry skin, mouth or lips
- nose bleeds
- dryness or runny nose
- an autoimmune disease where your own immune system attacks parts of your body by mistake. It often causes rash and joint pain but other parts of the body may be affected. (your doctor may also call it lupus or SLE)
- arthritis or joint pain
- kidney failure or worsening of kidney function (mainly in cancer patients who already suffer from kidney disease)
- blood tests: showing changes in kidney function
- blood tests showing in changes in chemicals called uric acid and lactate dehydrogenase
- mania (episodes of exaggerated elevation of mood)

Very rare side effects (may affect up to 1 in 10,000 people):
- an autoimmune disease where your own immune system attacks the platelets (cells which control clotting) in your blood by mistake. It can cause a severe decrease in the number of platelets and you may develop tiny bruise like spots on your skin
- sarcoidosis (a disease that results from inflammation of tissues of the body; sarcoidosis can affect almost any part of the body, but most often starts in the lungs or lymph nodes)
- hypertriglyceridaemia and hyperlipidaemia (high levels of some lipids/fats in the blood)
- damage to the retina (the back of the eye) or the blood vessels within the retina (can lead to blurred vision or in serious cases to loss of eyesight).
- your doctor may notice changes to the retina on examination of the eye including swelling of the main nerve at the back of the eye
- problems with eyesight related to the main nerve at the back of the eye
- worsening or return of a peptic ulcer and intestinal bleeding
- the area of skin where Roferon-A was injected may have redness, swelling and pain, and may cause a dead patch of skin around the injection site.
- problems related to mental state such as difficulty with thinking, concentration, personality changes or level of consciousness. Your doctor may call this encephalopathy.

Side effects for which the frequency cannot be determined:
- transplant rejections
- ischaemic colitis (insufficient blood supply to the bowels) and ulcerative colitis. Abdominal pain, bloody diarrhoea and fever are typical colitis signs.

Your doctor may decide to combine your Roferon-A treatment with other medicines. In such cases you may experience additional undesirable effects. Where these occur, they will be explained to you by your doctor.

Reporting of side effects
If you get any side effects talk to your doctor or pharmacist. This includes any possible side effects not listed in this leaflet. You can also report side effects directly (see details below). By reporting side effects you can help provide more information on the safety of this medicine.

Ireland
HPRA Pharmacovigilance
Earlsfort Terrace
IRL - Dublin 2
Tel: +353 1 6764971
Fax: +353 1 6762517
Website: www.hpra.ie
e-mail: medsafety@hpra.ie

United Kingdom
Yellow Card Scheme
Website: www.mhra.gov.uk/yellowcard

5. How to Store Roferon-A

Keep this medicine out of the sight and reach of children.

Do not use this medicine after the expiry date, which is stated on the carton and on the label after EXP. The expiry date refers to the last day of that month.

Store in a refrigerator (2 ºC to 8 ºC). Do not freeze. Keep the pre-filled syringe in the outer carton in order to protect from light.

Do not use Roferon-A if you notice that the solution is cloudy, if it has floating particles or if the medicine is any colour besides colourless to slightly yellowish.

Do not throw away any medicines via wastewater or household waste. Ask your pharmacist how to throw away medicines that you no longer use. These measures will help protect the environment.

6. Contents of the pack and other information

What Roferon-A contains
- The active substance is interferon alfa-2a, at 3 million IU/0.5 ml, 4.5 million IU/0.5 ml, 6 million IU/0.5 ml, or 9 million IU/0.5 ml.
- The other ingredients are ammonium acetate, sodium chloride, benzyl alcohol (10 mg/1 ml), polysorbate 80, glacial acetic acid, sodium hydroxide and water for injections

What Roferon-A looks like and contents of the pack
Roferon-A is a solution for injection (0.5 ml in pre-filled syringes).

Pack sizes: Packs of 1, 5, 6, 12 or 30. Not all pack sizes may be marketed.
The solution is clear, colourless to slightly yellowish.

Marketing Authorisation Holder
Roche Products Limited
6 Falcon Way, Shire Park
Welwyn Garden City
AL7 1TW, United Kingdom

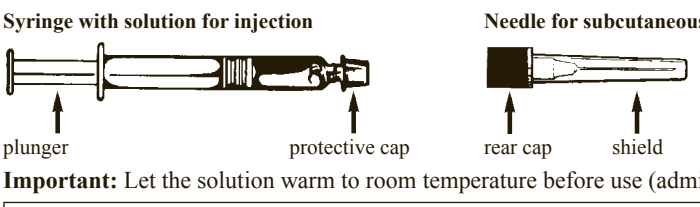
Manufacturer
Roche Pharma AG
Emil-Barell-Str. 1
D-79639 Grenzach-Wyhlen
Germany

This medicine is authorised in the Member States of the EEA under the following names:
Roferon-A: Austria, Belgium, Cyprus, Czech Republic, Estonia, Finland, Germany, Greece, Hungary, Ireland, Italy, Latvia, Lithuania, Luxemburg, Netherlands, Portugal, Slovakia, Slovenia, Spain, Sweden, United Kingdom.
Roféron-A: France.
Roceron-A: Norway.

This leaflet was last revised in:
March 2015

7. How to inject Roferon-A

Illustrated instructions for subcutaneous injection using Roferon®-A pre-filled syringe



Important: Let the solution warm to room temperature before use (administration).

1

Take the needle from the box. Take off the rear cap from the needle. Then, take the syringe from the box and take off the protective cap. Push the needle onto the syringe. Pull off the shield from the needle (see figure 1).

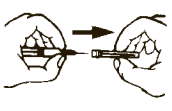


Figure 1.

2

Hold the syringe with the needle pointing up. Carefully push out any air by slowly pushing the plunger in.

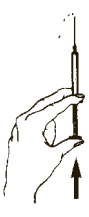


Figure 2.

3

Roferon-A can be injected either into the thigh or into the lower abdomen.
It is recommended that a new site be chosen for each injection

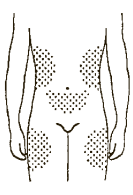


Figure 3.

4

Before injecting yourself, clean the injection site with an alcohol swab.

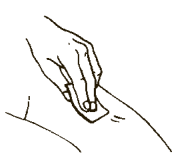


Figure 4.

5

Using your thumb and index finger, pinch up a fold of skin and insert the needle as far as it will go at an angle of 45 degrees (see figure 5).
Pull back the plunger of the syringe slightly.
If blood appears in the syringe, the needle has entered a blood vessel. If this happens you cannot inject the Roferon-A.
Discard the unused syringe and needle and start again with a new injection at a different site with a new syringe and needle.

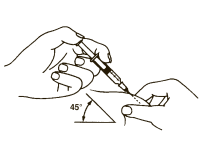


Figure 5.

6

Applying steady pressure, inject the contents of the Roferon-A pre-filled syringe beneath the skin until the syringe is completely empty.

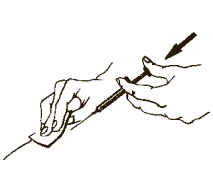


Figure 6.

7

To remove syringe, press the alcohol swab lightly on injection site and withdraw needle at a low angle.

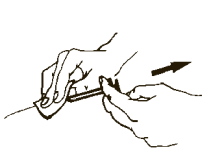


Figure 7.

The pre-filled syringes are for single use only. You should discard any unused product or waste material. Ask your doctor or pharmacist for future advice.

The following points should be strictly adhered to regarding the use and disposal of syringes and other medicinal sharps:
- Needles and syringes should never be reused.
- Place all used needles and syringes into a sharps container (puncture-proof disposable container).
- Keep this container out of the reach of children.
- Placing used sharps containers in the household waste should be avoided.
- Dispose of the full container according to local requirements or as instructed by your healthcare provider.