PATIENT PACKAGE INSERT IN ACCORDANCE WITH THE PHARMACISTS' REGULATIONS (PREPARATIONS) - 1986
The medicine is dispensed with a doctor's prescription only

Copegus®
200 mg
Film-coated Tablets

Composition:
Each tablet contains: ribavirin 200 mg
* For information on inactive ingredients, see section 6 - "Further Information".

Read this leaflet carefully in its entirety before using the medicine because it contains important information for you.
- Keep this leaflet. You may need to read it again.
- This leaflet contains concise information about the medicine. If you have further questions, refer to 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 it seems to you that their medical condition is similar.
- If you have side effects, refer to your doctor or pharmacist. This includes a possible side effect not mentioned in this leaflet (see section 4 – "Side Effects").

IMPORTANT INFORMATION FOR YOUR REVIEW
- **Copegus®** is given as part of a combination therapy with peginterferon alfa-2a or with interferon alfa-2a, to treat chronic hepatitis C.
- This medicine is not intended for children and adolescents under the age of 18.
- **Copegus®** may be very harmful to an unborn child. Therefore, it is very important for women treated with **Copegus®** to avoid becoming pregnant during the course of treatment and during the 4 months after treatment (see section "Pregnancy and breast-feeding").
- Adherence to the doctor's instructions (dosage and duration of treatment) increases the efficacy of the treatment. In any case, do not discontinue treatment without consulting your doctor. Please see sections 2 and 4 for detailed safety information.

1) WHAT IS THE MEDICINE INTENDED FOR?
Ribavirin, which is the active antiviral substance of **Copegus®**, inhibits the multiplication of many types of viruses, including viruses which cause chronic hepatitis C.
Copegus® is given as part of a combination therapy with peginterferon alfa-2a or with interferon alfa-2a, to treat chronic hepatitis C (a viral infection of the liver). It is given to adult patients who have or have not been previously treated for chronic hepatitis C.
The medicine is also intended, in combination with peginterferon alfa-2a, for the treatment of co-infection with HIV and chronic hepatitis C.
Copegus® should be used only in combination with peginterferon alfa-2a or interferon alfa-2a. Do not take **Copegus®** alone.
Read carefully the peginterferon alfa-2a or interferon alfa-2a patient leaflet as well before commencing treatment.

Therapeutic group
Nucleoside inhibitor-type antiviral medicines.

2) BEFORE USING THE MEDICINE
Do not use the medicine if:
- you are sensitive (allergic) to ribavirin or to any of the other ingredients of this medicine (see section 6 – "Further Information").
- you are pregnant or if you are breast-feeding (see section "Pregnancy and breast-feeding").
- you have had a heart attack or have suffered from other severe heart disease in the previous six months.
- you suffer from advanced liver disease (for example, if your skin has become yellow and you have excess fluid in the abdomen).
- you suffer from blood disorder such as thalassemia or sickle cell anemia (weakening and destruction of the red blood cells).
- you are co-infected with HIV and chronic hepatitis C, and also suffer from advanced liver disease - in some cases, treatment with **Copegus®** in combination with peginterferon alfa-2a should not be started. Your attending doctor will determine if this is the case.

Read the peginterferon alfa-2a or interferon alfa-2a patient leaflet as well for further information.

Special warnings regarding use of the medicine
Do not use the medicine without consulting the doctor before commencing treatment:
- if you are a woman of child-bearing age (see section "Pregnancy and breast-feeding").
- if you are a man and your female partner is of child-bearing age (see section "Pregnancy and breast-feeding").
- if you suffer from a heart problem. In a case like this, you will need to be monitored. It is recommended to have a heart recording (E.C.G. or electrocardiogram) prior to and during treatment.
- if you develop a heart problem along with intense fatigue. This can be caused by anemia as a result of treatment with **Copegus®**.
- if you have ever had anemia (the risk of developing anemia is generally higher in women compared to men).
- if you suffer from kidney problem. The **Copegus®** dosage may need to be decreased.
- if you underwent an organ transplantation (such as liver or kidney transplantation) or have such a transplantation planned in the near future.
- if you develop symptoms of an allergic reaction, such as: difficulty in breathing, wheezing, sudden swelling of the skin and mucous membranes, itching or rash; stop **Copegus®** treatment immediately and seek medical help right away.
- if you have suffered in the past from depression or developed symptoms associated with depression (e.g., feeling of sadness, dejection, and the like) while on treatment with **Copegus®** (see section 4 - "Side Effects").
- if you currently have, or have had in the past, an addiction problem (e.g., addiction to alcohol or to drugs).
- if you are under the age of 18. The efficacy and safety of **Copegus®** in combination with peginterferon alfa-2a or interferon alfa-2a have not been sufficiently evaluated in patients under the age of 18.
- if you are co-infected with HIV and are being treated with any anti-HIV medicinal products.
- if you have discontinued previous treatment for chronic hepatitis C because of anemia or low blood count.
- if you are over 65 years of age.

If you are a woman of child-bearing age, you must perform a pregnancy test before starting treatment with **Copegus®**, once a month during treatment and during the 4 months after completing treatment (see section "Pregnancy and breast-feeding").
The following severe side effects are associated in particular with combination therapy of **Copegus®** with interferon alfa-2a or peginterferon alfa-2a; please refer to the package leaflets of these medicinal products for more detailed information on the following safety issues:
- Psychiatric and central nervous system effects (such as depression, suicidal thoughts, attempted suicide and aggressive behaviour, etc.). Proceed to an emergency room if you feel depressed, have suicidal thoughts or if your behaviour changes. You may want to consider asking a family member or close friend to help you stay alert to signs of depression or changes in your behaviour.
- Severe ocular disorder.
- Dental and periodontal disorders - Dental and gum disorders have been reported in patients receiving **Copegus®** and peginterferon alfa-2a combination therapy. Brush your teeth thoroughly twice daily and have regular dental examinations. In addition, some patients may suffer from vomiting. If you suffer from vomiting, rinse out your mouth thoroughly afterwards.
- Growth inhibition in children and adolescents that may be irreversible in some patients.

Copegus® and other medicines
If you are taking, or have recently taken, other medicines, including non-prescription medicines and nutritional supplements, inform the doctor or pharmacist. It is especially important to inform the doctor or pharmacist if you are taking:
Anti-HIV medicines, such as: zidovudine, stavudine, azathioprine and didanosine.
Lactic acidosis (a build up of lactic acid in the body that causes the blood to become acidic) and worsening liver function are side effects associated with HAART (Highly Active Anti-Retroviral Therapy), an HIV treatment regimen. If you are being treated with HAART, the addition of **Copegus®** to peginterferon alfa-2a or interferon alfa-2a may increase your risk of lactic acidosis or liver failure. The attending doctor will monitor you for signs and symptoms of these conditions.
If you are taking zidovudine or stavudine because you are HIV-positive or are suffering from AIDS: **Copegus®** may decrease the effect of these medicines. Therefore, blood tests should be performed regularly to make sure the HIV infection is not getting worse. If it does get worse, your doctor may decide to stop treatment with **Copegus®**. In addition, patients receiving zidovudine in combination with **Copegus®** and alfa interferons are at increased risk of developing anemia.
Co-administration of **Copegus®** and didanosine (which is used to treat HIV) is not recommended. Certain side effects of didanosine (e.g., liver problems, tingling and pain in the arms and/or feet, pancreatitis) may occur more frequently.
Patients receiving azathioprine in combination with **Copegus®** and peginterferon are at high risk of developing severe blood system disorders.
Carefully read the patient leaflet for peginterferon alfa-2a or interferon alfa-2a, to ensure you know which medicines you can take while you are taking either of these medicines.
Copegus® may remain in your body for two months; therefore, consult with your attending doctor or pharmacist before starting treatment with any of the medicines mentioned in this leaflet.

Use of the medicine and food
Copegus® tablets are usually taken twice a day (morning and evening) with food and should be swallowed whole.

Pregnancy and breast-feeding
If you are pregnant or breast-feeding, think you may be pregnant or are planning to become pregnant, consult the doctor or pharmacist before taking medicines.
If you are pregnant or breast-feeding, think you may be pregnant or are planning to become pregnant, consult the doctor or pharmacist before taking this medicine.
Copegus® can be very harmful to an unborn child; it may cause birth defects. Therefore, it is very important that **women taking Copegus®** avoid becoming pregnant during treatment and during the 4 months after treatment.
Copegus® can damage the sperm and thereby harm the unborn child. Therefore, it is very important that female partners of **men taking Copegus®** avoid becoming pregnant during the course of treatment and during the 7 months after treatment of the male.
If you are **a woman** of child-bearing age who is taking **Copegus®**, you must rule out pregnancy before starting treatment (negative pregnancy test), once a month during therapy and during the 4 months after treatment is stopped. You must use an effective contraceptive during the entire period you are taking **Copegus®** and for 4 months after stopping treatment. This can be discussed with your doctor. If your male partner is being treated with **Copegus®**, read the next paragraph "If you are **a man**".
If you are **a man** who is taking **Copegus®**, do not have sex with a pregnant woman without using 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 child-bearing age, she must perform a pregnancy test once a month during the entire course of your treatment with **Copegus®** and for the 7 months after treatment is discontinued. You or your female partner must use an effective contraceptive during the entire period that you are taking **Copegus®** and for 7 months after stopping treatment. This can be discussed with your doctor. If your female partner is being treated with **Copegus®**, read the paragraph "if you are **a woman**".
It is not known whether **Copegus®** is excreted into breast milk. Do not breast-feed during the course of treatment with **Copegus®**, as this may harm the baby. If treatment with **Copegus®** is necessary, stop breast-feeding.

Driving and using machines
Treatment with **Copegus®** has very little effect on the ability to drive or use machines.
However, peginterferon alfa-2a or interferon alfa-2a may cause sleepiness, tiredness or confusion. Do not drive a car and do not use tools or machines, if you develop any of these symptoms.

3) HOW SHOULD YOU USE THE MEDICINE?
Always use this medicine exactly according to the doctor's instructions. Check with the doctor or pharmacist if you are not sure. Your doctor will determine the correct dosage for you, depending on your weight, the type of virus you suffer from and the medicine you are taking concomitantly with **Copegus®**.
Recommended dosage
The dosage and the treatment regimen will be determined by the doctor only. **Do not exceed the recommended dose.**
The recommended dosage of **Copegus®** ranges between 800 and 1,200 mg per day.
The duration of treatment varies, depending on the type of virus that caused the infection, on response to treatment, if you have already received treatment for your disease in the past and if there is co-infection with HIV.
Use this medicine at regular intervals, as determined by your doctor.
Copegus® tablets are usually taken twice a day (morning and evening).
Swallow the tablets whole with food.
Do not chew!
Do not crush or halve the tablets!
As ribavirin is a teratogenic substance (may cause birth defects), the tablets should be handled with care **and should not be halved or crushed.** If you accidentally touch damaged tablets, thoroughly wash with soap and water all parts of your body which came in contact with the contents of the tablets. If any powder from the tablets gets in your eyes, rinse your eyes thoroughly with sterile water, or tap water, if sterile water is not available.
If you have the impression that the effect of **Copegus®** is too strong or too weak, refer to your doctor or pharmacist.
If side effects occur during treatment, your doctor may adjust the dosage or stop treatment.
Copegus® is administered in combination with peginterferon alfa-2a or interferon alfa-2a. Refer to the patient leaflet for peginterferon alfa-2a or interferon alfa-2a as well for the dosage of these medicines.
Tests and monitoring
Before starting treatment with **Copegus®**, kidney function must be tested in all patients, and blood tests should be conducted as well. The blood tests should be repeated after 2 and 4 weeks of treatment, and thereafter, at a frequency determined by your doctor.
During the course of treatment with **Copegus®**, your doctor will regularly perform blood tests to monitor changes in the number of white blood cells (cells that fight infections), red blood cells (cells that carry oxygen), platelets (cells responsible for blood clotting), liver function or changes in other laboratory values.
If you accidentally take too high a dosage, contact the doctor or pharmacist as soon as possible.
If you took an overdose or if a child 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 forget to take this medicine at the required time, take it as soon as you remember and take the next dose at its regular scheduled time. Do not take a double dose to compensate for the forgotten dose.
Adhere to the treatment regimen as recommended by the doctor.
Discontinuation of treatment: Even if there is an improvement in your health, do not discontinue treatment with the medicine without consulting the doctor or pharmacist.
Only your doctor can decide how to discontinue your treatment. Do not discontinue treatment without consulting a doctor, as the disease for which you are being treated may recur or get worse.
How can you contribute to the success of the treatment?
Even if there is an improvement in your health, do not discontinue treatment with the medicine without consulting a doctor.
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 the medicine, consult the doctor or pharmacist.

4) SIDE EFFECTS
Like all medicines, the use of **Copegus®** 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.
Report to your doctor immediately if you notice the following side effects: severe pain in chest area; persistent cough; irregular heartbeat; trouble breathing; confusion; depression; severe stomach pain; blood in stools (or black stools); severe nosebleed; fever or chills; eyesight problems.
All these side effects may occur when taking **Copegus®** in combination with peginterferon alfa-2a or interferon alfa-2a. These side effects may be serious and you may need urgent medical attention.
Additional side effects:
Very common side effects when combining **Copegus®** with peginterferon alfa (may affect more than 1:10 patients):
Anemia (low red blood cell count), neutropenia (low white blood cell count); loss of appetite; feeling depressed (feeling low, feeling bad about yourself or feeling hopeless), inability to sleep; headaches, difficulty concentrating and dizziness; cough, shortness of breath; diarrhea, nausea, abdominal pain; loss of hair, skin reactions (e.g., itchiness, dermatitis, and dry skin); pain in joints and muscles; fever, weakness, tiredness, shaking, chills, pain, and irritability (tendency to get upset easily).

Common side effects when combining **Copegus®** with peginterferon alfa (may affect up to 1:10 patients):
Upper respiratory tract infection, bronchitis, fungal infection of the mouth, herpes (a common recurring viral infection affecting the lips and mouth); low platelet count (affects blood clotting ability), enlarged lymph glands; overactive and underactive thyroid gland; emotional or mood changes, anxiety, aggression, nervousness, decreased sexual desire; reduced memory, fainting, decreased muscle strength, migraines, numbness, tingling, burning sensation, tremor, changes in the sense of taste, nightmares, sleepiness; blurry vision, eye pain, eye inflammation, dry eyes; sensation of room spinning, ear pain, ringing in the ears; rapid heart rate, palpitations, swelling in the extremities; flushing, low blood pressure; shortness of breath upon exertion, nose bleeds, nose and throat inflammation, infections of the nose and sinuses (air-filled spaces found in the bones of the face and head), runny nose, sore throat; vomiting, indigestion, difficulty swallowing, mouth ulceration, bleeding gums, inflammation of the tongue and mouth, excess amount of air or gas in the abdomen, constipation, dry mouth; rash, increased sweating, psoriasis, hives, eczema, sensitivity to sunlight, night sweats; back pain, joint inflammation, muscle weakness, bone pain, neck pain, muscle pain, muscle cramps; impotence (inability to maintain an erection); chest pain, flu-like illness, malaise, lethargy, hot flushes, thirst and weight loss.

Uncommon side effects when combining **Copegus®** with peginterferon alfa (may affect up to 1:100 patients):
Lower respiratory tract infections, urinary tract infections, skin infections; sarcoidosis (areas of inflamed tissue occurring throughout the body), inflammation of the thyroid gland; diabetes (high blood sugar level); dehydration; suicidal thoughts, hallucinations, anger; hearing loss; peripheral neuropathy (disorder of the nerves affecting the extremities); bleeding in the retina (the back part of the eye); high blood pressure; wheezing; gastrointestinal bleeding, inflammation of the lips, inflammation of the gums; reduced functioning of the liver.

Rare side effects when combining **Copegus®** with peginterferon alfa (may affect up to 1:1,000 patients):
Infection of the heart, infection of the external ear; severe reduction in the number of red blood cells, white blood cells and platelets; severe allergic reaction, systemic lupus erythematosus (an illness where the body attacks its own cells), rheumatoid arthritis (an autoimmune disease); suicide, psychotic disorders (severe personality disturbances and deterioration in normal social functioning); coma (a deep prolonged unconsciousness), seizures, facial palsy; inflammation and swelling of the optic nerve, inflammation of the retina, ulceration of the cornea; heart attack, heart failure, pain in heart area, rapid heart rhythm, heart rhythm disorders, inflammation of the lining of the heart; bleeding in the brain, vasculitis (inflammation of the blood vessels); interstitial pneumonia (inflammation of the lungs which may be fatal), blood clots in the lungs; stomach ulcer, pancreatitis; liver failure, bile duct inflammation, fatty liver; inflammation of the muscles; substance overdose.

Very rare side effects when combining **Copegus®** with peginterferon alfa (may affect up to 1:10,000 patients):
Aplastic anemia (failure of the bone marrow to produce red blood cells, white blood cells and platelets); ITP or TTP (a disease which is manifested by increased bruising, bleeding, decreased platelet count, anemia and extreme weakness); loss of vision; stroke; a spectrum of rashes with varying degrees of severity, which may be associated with blisters in the mouth, nose, eyes and other mucosal membranes (Toxic epidermal necrolysis/Stevens Johnson syndrome/Erythema multiforme), angioedema (a disease manifested by swelling in the skin and mucous membranes).

Side effects with unknown frequency:
Pure Red Cell Aplasia (a severe form of anemia where red blood cell production is decreased or stopped), this effect may result in symptoms such as feeling very tired and lack of energy; liver or kidney transplant rejection; Vogt Koyanagi Harada Syndrome (a rare disease characterized by loss of vision, loss of hearing and appearance of skin pigmentation); mania (episodes of exaggerated elevation of mood) and bipolar disorders (episodes of exaggerated elevation of mood alternating with sadness and hopelessness); a rare form of retinal detachment with fluid in the retina; ischemic colitis (insufficient blood supply to the bowels), ulcerative colitis (an inflammation of the large intestine that causes ulcers, resulting in diarrhea), tongue discoloration; serious muscle damage and pain; inadequate kidney functioning, any evidence of another kidney problem.
If you are co-infected with HIV and chronic hepatitis C, and are receiving HAART (Highly Active Anti-Retroviral Therapy), the addition of **Copegus®** to peginterferon alfa-2a or interferon alfa-2a may cause the following side effects: fatal liver failure, peripheral neuropathy (numbness, tingling or pain in hands or feet), pancreatitis (possible symptoms: acute upper abdominal pain, nausea and vomiting), lactic acidosis (a build up of lactic acid in the body, causing the blood to become acidic), influenza, pneumonia, alterations in mood, apathy (lethargy), pain in the back of the mouth and throat, dry and cracked lips, increased amount of fat in the upper back and in the neck and changes in color of the urine.
If you experience side effects, talk to the doctor or pharmacist. This includes any possible side effect not listed in this leaflet; you should consult the doctor.
Read the patient leaflet for peginterferon alfa-2a or interferon alfa-2a as well for additional information regarding side effects of the relevant product.

Reporting side effects
Side effects can be reported to the Ministry of Health by clicking on the link "Reporting side effects following drug treatment" found on the Ministry of Health homepage (www.health.gov.il) that directs you to the online form for reporting side effects,
or by entering the link:
https://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 must be kept in a safe place out of the reach of children and/or infants 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. In any case of doubt, consult the pharmacist who dispensed the medicine to you.
- Storage conditions: Do not store above 30°C.
- Shelf life after first opening: 168 days (24 weeks).
- Do not use **Copegus®** if the bottle or package has been damaged.
- Child-proof caps have significantly lowered the number of cases of poisoning caused annually by medicines. However, if you find it difficult to open the package, you can refer to the pharmacist and request that the safety mechanism on the cap be removed and to turn it into a regular, easy-to-open cap.

Do not discard the medicine via household waste or wastewater. Ask the pharmacist how to discard the medicine in order to protect the environment.

6) FURTHER INFORMATION
In addition to the active ingredient, the medicine also contains:
Tablet core: pregelatinized starch, sodium starch glycolate (type A), microcrystalline cellulose, maize starch, magnesium stearate.
Film-coating: hypromellose, talc, titanium dioxide, yellow iron oxide, red iron oxide, ethylcellulose aqueous dispersion, triacetin.
What does the medicine look like and what are the contents of the package?
The tablets are light pink, flat, oval-shaped and film-coated ("RIB 200" is imprinted on one side and "ROCHE" is imprinted on the other side).
Copegus® 200 mg tablets are available in bottles containing 42, 112 and 168 tablets*.
* Not all package sizes may be available.
Manufacturer and address: F. Hoffmann-La Roche Ltd., Basel, Switzerland.
License holder and address: Roche Pharmaceuticals (Israel) Ltd., P.O.B. 6391, Hod Hasharon 4524079.
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