Package leaflet: Information for the patient

Copegus 400 mg film-coated tablets

Ribavirin

Read all of this leaflet carefully before you start taking 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 Copegus is and what it is used for
2. What you need to know before you take Copegus
3. How to take Copegus
4. Possible side effects
5. How to store Copegus
6. Contents of the pack and other information

1. What Copegus is and what it is used for

Ribavirin, which is the antiviral active substance of Copegus, inhibits the multiplication of many types of viruses, including the hepatitis C viruses (which can cause an infection of the liver called hepatitis C).

Copegus is used in combination with other medicines to treat certain chronic forms of hepatitis C.

Copegus should only be used in combination with other medicines to treat hepatitis C. It should not be taken alone.

Refer also to the package leaflets of the other medicines that are used in combination with Copegus.

2. What you need to know before you take Copegus

Do not take Copegus:
- if you are allergic to ribavirin or to any of the other ingredients of this medicine (listed in section 6).
- if you are pregnant or breast-feeding (see section "Pregnancy and breast-feeding").
- if you have had a heart attack or have suffered from any other severe heart disease in the previous six months.
- if you have a blood disorder such as sickle cell anaemia or thalassaemia (weakening and destruction of red blood cells).

Refer also to the package leaflets of the other medicines that are used in combination with Copegus. Do not take Copegus in combination with medicines called interferons or pegylated interferons if you have advanced liver disease (e.g. your skin has become yellow and you have excess fluid in your abdomen).

Warnings and precautions

Talk to your doctor before taking Copegus
- 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 childbearing age (see section "Pregnancy and breast-feeding").
- if you have a heart problem. In this case you will need to be monitored carefully. A heart recording (ECG or electrocardiogram) is recommended prior to and during treatment.
- if you develop a heart problem along with intense fatigue. This may be due to anaemia caused by Copegus.
- if you have ever had anaemia (the risk of developing anaemia is higher in women compared to men, in general).
- if you have a problem with your kidneys. Copegus treatment may need to be decreased.
- if you have had an organ transplant (such as liver or kidney) or have one 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 rashes. Copegus treatment must be stopped immediately and you should seek medical help immediately.
- if you have ever had depression or develop symptoms associated with depression (e.g. feelings of sadness, dejection, etc) while on treatment with Copegus (see section 4).
- if you are an adult who has or had a history of substance abuse (e.g. alcohol or 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 years.
- if you are co-infected with HIV and are being treated with any anti HIV medicinal products.
- if you have been withdrawn from previous therapy for hepatitis C because of anaemia or low blood count.

Before treatment with Copegus, kidney function must be tested in all patients. Your doctor must also test your blood before starting treatment with Copegus. The blood tests should be repeated after 2 and 4 weeks of treatment, and thereafter as frequently as your doctor thinks is necessary.

If you are a woman of childbearing age, you must have a pregnancy test before starting treatment with Copegus, every month during treatment and during the 4 months after treatment (see section "Pregnancy and breast-feeding").

The following severe side effects are associated in particular with Copegus use in combination with interferon alfa-2a or peginterferon alfa-2a, please refer to the package leaflet of these medicinal products for more detailed information on these safety issues:

- Psychiatric and central nervous system effects (such as depression, suicidal thoughts, attempted suicide and aggressive behavior, etc.). Be sure to seek emergency care if you notice that you are becoming depressed or have suicidal thoughts or change in your behaviour. 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. You should brush your teeth thoroughly twice daily and have regular dental examinations. In addition some patients may experience vomiting. If you have this reaction, be sure to rinse your mouth thoroughly afterwards
- Growth inhibition in children and adolescents that may be irreversible in some patients

Other medicines and Copegus
Tell your doctor or pharmacist if you are taking, have recently taken or might take any other medicines.

Patients who also have HIV infection: Tell your doctor if you are being treated for HIV.

Lactic acidosis (a build up of lactic acid in the body, leading to the blood becoming acidic) and worsening liver function are side effects associated with HAART (Highly Active Anti-Retroviral Therapy), an HIV treatment regimen. If you are receiving HAART, the addition of Copegus to peginterferon alfa-2a or interferon alfa-2a may increase your risk of lactic acidosis or liver failure. Your doctor will monitor you for signs and symptoms of these conditions.

If you take zidovudine or stavudine, because you are HIV positive or suffering from AIDS it is possible that Copegus can decrease the effect of these medicines. Therefore your blood will be checked regularly to make sure the HIV infection is not getting worse. If it does get worse, your doctor may decide to stop your treatment with Copegus. In addition, patients receiving zidovudine in combination with Copegus and alfa interferons are at increased risk of developing anaemia.

Co-administration of Copegus and didanosine, (which is a treatment for HIV) is not recommended. Certain side effects of didanosine (e.g. liver problems, tingling and painful arms and /or feet, pancreatitis) may occur more frequently.

Patients receiving azathioprine in combination with Copegus and peginterferon are at increased risk of developing severe blood disorders.

Refer also to the package leaflets of the other medicines that are used in combination with Copegus.

Ribavirin may remain in your body for up to 2 months, therefore you should check with your doctor or pharmacist before starting treatment with any of the other medicines mentioned in this leaflet.

Copegus with food and drink

Copegus film-coated tablets are normally taken at two times in the day with food (morning and evening) 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 have a baby, ask your doctor or pharmacist for advice before taking this medicine.

Copegus can be very harmful to the unborn child; it may cause birth defects. Therefore, if you are a **female patient,** it is very important to avoid becoming pregnant during treatment and during the 4 months after treatment. Copegus can damage the sperm and so harm the embryo (unborn child). Therefore, if you are a **male patient,** it is very important for your female partner to avoid becoming pregnant during your treatment and during the 7 months after treatment.

If you are a **woman** of childbearing age who is taking Copegus, you must have a negative pregnancy test before treatment, each month during therapy and for the 4 months after treatment is stopped. You must 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 your male partner is being treated with Copegus, please see the section "If you are a **man**".

If you are a **man** who is taking Copegus, do not have sex with a pregnant woman 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 the 7 months after treatment has stopped. You or your partner must use an effective contraceptive during the time you are taking the treatment and for 7 months after stopping treatment. This can be discussed with your doctor. Please see "if you are a **woman"** if your female partner is treated with Copegus

If you are pregnant or breast feeding, think you may be pregnant or are planning to have a baby, ask your doctor or pharmacist for advice before taking this medicine.

It is not known whether Copegus is excreted in human milk. Women should not breast-feed while taking Copegus as this may harm the baby. If treatment with Copegus is necessary, breast-feeding should be stopped.

Refer also to the package leaflets of the other medicines that are used in combination with Copegus for the treatment of hepatitis C.

Driving and using machines

Copegus has very little effect on your ability to drive or use machines.
However, the other medicines you take with Copegus may have an effect. Check the package leaflets of the other medicines you are using in combination with Copegus.

3. How to take Copegus

Always take this medicine exactly as your doctor has told you. Check with your doctor or pharmacist if you are not sure. Your doctor will decide the correct dose for you depending on your body weight, type of virus, and the medicine you take in combination with Copegus.

The recommended dose ranges between 800mg to 1400 mg/day depending on the other medicines you are using in combination with Copegus.
- 800 mg/day: Take 1 Copegus 400 mg tablet in the morning and 1 tablet in the evening
- 1000 mg/day: Patients are advised to take Copegus 200 mg tablets
- 1200 mg/day: Patients are advised to take Copegus 200 mg tablets
- 1400 mg/day: Patients are advised to take Copegus 200 mg tablets

In the case of combination therapy with other medicines, please follow the dosing regimen recommended by your doctor and refer also to the package leaflets of the other medicines.

Swallow the tablets whole and take the tablets with food.

As ribavirin is teratogenic (may cause abnormalities in the unborn child), the tablets should be handled with care **and should not be broken or crushed.** If you accidentally touch damaged tablets, wash thoroughly with soap and water any part of your body which came in contact with the contents of the tablet. If any powder from the tablets gets in your eyes, rinse your eyes thoroughly with sterile water, or plain water if sterile water is not available.

The amount of time you have to continue taking Copegus film-coated tablets varies, depending on, the type of virus you are infected with, which other medicine you are being treated with, on treatment response and whether you have been treated before. Please check with your doctor and follow the recommended duration of treatment.

If you are over the age of 65 you should consult your doctor before using Copegus.

If you have the impression that the effect of Copegus is too strong or too weak, talk to your doctor or pharmacist.

If side-effects occur during treatment, your doctor may adapt the dose or stop treatment.

Refer also to the package leaflets of the other medicines that are used in combination with Copegus.

If you take more Copegus than you should

Contact your doctor or pharmacist as soon as possible.

If you forget to take Copegus

Do not take a double dose to make up for a forgotten dose.
If you miss a dose, take it as soon as you remember and take the next dose at the normal time.

If you stop taking Copegus

Only your doctor can decide when your treatment should be discontinued. Never stop the treatment yourself because the disease, for which you are being treated, can come back or get worse.

If you have any further questions on the use of this medicine, ask your doctor or pharmacist.

4. Possible side effects

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

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 below). By reporting side effects you can help provide more information on the safety of this medicine.

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During treatment, your doctor will take blood samples regularly to check for changes in your white blood cells (cells that fight infection), red blood cells (cells that carry oxygen), platelets (blood clotting cells), liver function or changes in other laboratory values.

Refer also to the package leaflets of the other medicines that are used in combination with Copegus for information on the side effects for those products.

The side effects listed in this section were observed primarily when Copegus was used in combination with interferon alfa-2a or peginterferon alfa-2a.

Tell your doctor immediately if you notice any of the following side effects occur: severe chest pain; persistent cough; irregular heartbeat; trouble breathing; confusion; depression; severe stomach pain; blood in stools (or black, tarry stools); severe nosebleed; fever or chills; problems with your eyesight. These side effects can be serious and you may need urgent medical attention.

Very common side effects with the combination of pegylated alfa interferon and ribavirin (may affect more than 1 in 10 people) are:
Blood disorders: Anaemia (low red cell count), neutropenia (low white blood cell count)
Metabolic disorders: Loss of appetite
Psychiatric disorders: Feeling depressed (feeling low, feeling bad about yourself or feeling hopeless), inability to sleep
Nervous system disorders: Headache, difficulty concentrating and dizziness
Respiratory disorders: Cough, shortness of breath

Gastrointestinal disorders: Diarrhoea, nausea, abdominal pain
Skin disorders: Loss of hair, and skin reactions (including itching, dermatitis and dry skin)
Musculoskeletal disorders: Pain in joints and muscles
General disorders: Fever, weakness, tiredness, shaking, chills, pain, and irritability (getting easily upset)

Common side effects with the combination of pegylated alfa interferon and ribavirin (may affect up to 1 in 10 people):
Infections: Upper respiratory infection, bronchitis, fungal infection of the mouth and herpes (a common recurring viral infection affecting the lips, mouth)
Blood disorders: Low platelet count (affecting the clotting ability) and enlarged lymph glands
Endocrine disorders: Overactive and underactive thyroid gland
Psychiatric disorders: Mood /emotion changes, anxiety, aggression, nervousness, decreased sexual desire
Nervous system disorders: Poor memory, fainting, decreased muscle strength, migraine, numbness, tingling, burning sensation, tremor, changes in the sense of taste, nightmares, sleepiness
Eye Disorders: Blurry vision, eye pain, eye inflammation and dry eyes
Ear disorders: Sensation of room spinning, ear pain, ringing in ears
Cardiac disorders: Rapid heart rate, pulsation of the heart beats, swelling in the extremities
Vascular disorders: Flushing, low blood pressure
Respiratory disorders: Shortness of breath with activity, nose bleeds, nose and throat inflammation, infections of the nose and sinuses (air-filled spaces found in the bones of the head and face), runny nose, sore throat
Gastrointestinal disorders: Vomiting, indigestion, difficulty swallowing, mouth ulceration, bleeding gums, inflammation of tongue and mouth, flatulence (excess amount of air or gases), constipation, dry mouth
Skin disorders: Rash, increased sweating, psoriasis, hives, eczema, sensitivity to sunlight, night sweats
Musculoskeletal disorders: Back pain, joint inflammation, muscle weakness, bone pain, neck pain, muscle pain, muscle cramps
Reproductive system disorders: Impotence (inability to maintain an erection)
General disorders: Chest pain, flu-like illness, malaise (not feeling well), lethargy, hot flushes, thirst, weight decreased

Uncommon side effects with the combination of pegylated alfa interferon and ribavirin (may affect up to 1 in 100 people):
Infections: Lower respiratory tract infections, urinary tract infection, skin infections
Immune disorders: Sarcoidosis (areas of inflamed tissue occurring throughout the body), inflammation of the thyroid
Endocrine disorders: Diabetes (high blood sugar)
Metabolic disorders: Dehydration
Psychiatric disorders: Thoughts of suicide, hallucinations (abnormal perceptions), anger
Nervous system disorder: Peripheral neuropathy (disorder of the nerves affecting the extremities)
Eye disorder: Bleeding in the retina (back of the eye)
Ear and labyrinth disorders: Hearing loss
Vascular disorder: High blood pressure
Respiratory disorder: Wheezing
Gastrointestinal disorders: Gastrointestinal bleeding, inflammation of the lips, inflammation of the gums
Liver disorders: Poor functioning of the liver

Rare side effects with the combination of pegylated alfa interferon and ribavirin (may affect up to 1 in 1000 people):
Infections: Infection of the heart, infection of the external ear
Blood disorders: Severe reduction in red blood cells, white blood cells and platelets
Immune system disorders: Severe allergic reaction, systemic lupus erythematosus (an illness where the body attacks its own cells), rheumatoid arthritis (an autoimmune disease)

Psychiatric disorders: Suicide, psychotic disorders (severe problems with personality and deterioration in normal social functioning)
Nervous system disorders: Coma (a deep prolonged unconsciousness), seizures, facial palsy
Eye disorders: Inflammation and swelling of the optic nerve, inflammation of the retina, ulceration of the cornea
Cardiac disorders: Heart attack, heart failure, heart pain, rapid heart rhythm, rhythm disorders or inflammation of the lining of the heart
Vascular disorders: Bleeding in the brain, vasculitis (inflammation of the blood vessels)
Respiratory disorders: Interstitial pneumonia (inflammation of the lungs with fatal outcome), blood clots in the lung
Gastrointestinal disorders: Stomach ulcer, inflammation of the pancreas
Liver disorders: Liver failure, bile duct inflammation, fatty liver
Musculoskeletal disorders: Inflammation of the muscles
Injury or poisoning: Substance overdose

Very rare side effects with the combination of pegylated alfa interferon and ribavirin (may affect up to 1 in 10,000 people):
Blood disorders: Aplastic anaemia (failure of the bone marrow to produce red blood cells, white blood cells and platelets)
Immune System disorders: Idiopathic (or thrombotic) thrombocytopenic purpura (increased bruising, bleeding, decreased platelets, anaemia and extreme weakness)
Eye disorders: Loss of vision
Nervous System Disorders: Stroke
Skin disorders: Toxic epidermal necrolysis/ Stevens Johnson Syndrome/ erythema multiforme (a spectrum of rashes with varying degrees of severity which may be associated with blisters in the mouth, nose, eyes and other mucosal membranes), angioedema (swelling in the skin and mucosa)

Side effects with unknown frequency:
Blood disorders: Pure red cell aplasia (a severe form of anaemia where red blood cell production is decreased or stopped); it can result in symptoms such as feeling very tired with no energy
Immune System disorders: liver and kidney transplant rejections, Vogt Koyanagi Harada Syndrome – a rare disease characterised by loss of vision, hearing, and skin pigmentation
Psychiatric disorders: mania (episodes of exaggerated elevation of mood) and bipolar disorders (episodes of exaggerated elevation of mood alternating with sadness or hopelessness)
Eye disorders: Rare form of retinal detachment with fluid in the retina
Digestive system disorders: Ischemic colitis (insufficient blood supply to the bowels), ulcerative colitis (inflammation of the large intestine that causes ulcers, resulting in diarrhoea), change in colour of the tongue
Musculoskeletal disorders: Serious muscle damage and pain
Renal disorders: kidneys stop functioning adequately, other complaints that suggest kidney problems

If you are infected with both viruses, HCV and HIV, and are receiving HAART (Highly Active Anti-Retroviral Therapy), the addition of Copegus to peginterferon alfa-2a or interferon alfa-2a therapy may cause fatal liver failure, peripheral neuropathy (numbness, tingling or pain in hands or feet), pancreatitis (symptoms may include stomach pain, nausea and vomiting), lactic acidosis (a build up of lactic acid in the body, leading to the blood becoming acidic), influenza, pneumonia, affect lability (alterations in mood), apathy (lethargy), pharyngolaryngeal pain (pain in the back of your mouth and throat), cheilitis (dry and cracked lips), acquired lipodystrophy (increased amount of fat in upper back and neck) and chromaturia (change in colour of your urine) as 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.

5. How to store Copegus

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 label. The expiry date refers to the last day of that month.

This medicinal product does not require any special storage conditions.

Do not use this medicine if you notice the bottle or packaging is damaged.

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

6. Contents of the pack and other information

What Copegus contains

- Each film-coated tablet contains 400 mg of ribavirin.
- The other ingredients are
  Tablet core: pregelatinised maize starch, sodium starch glycolate (type A), microcrystalline cellulose, maize starch, magnesium stearate
  Film coating: hypromellose, talc, titanium dioxide (E171) yellow iron oxide (E172), red iron oxide (E172), triacetin.

What Copegus looks like and contents of the pack

The tablets are reddish brown, flat oval-shaped film-coated tablets (marked with RIB 400 on one side and ROCHE on the opposite side).

Copegus 400 mg film-coated tablets are available in bottles containing 14 and 56 tablets. Not all sizes may be marketed.

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