Package leaflet: Information for the patient

Moderiba 200 mg film-coated tablets
Moderiba 400 mg film-coated tablets
Moderiba 600 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 Moderiba is and what it is used for

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

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

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

Please also read the package leaflets of the other medicines that are used in combination with Moderiba.

2. What you need to know before you take Moderiba

Do not take Moderiba:
- if you are allergic to ribavirin or 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).

Please also read the package leaflets of the other medicines that are used in combination with Moderiba.

Do not take Moderiba 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 Moderiba:
- 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 Moderiba.
- 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. Moderiba 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. Moderiba 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 Moderiba (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 Moderiba 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 Moderiba, kidney function must be tested in all patients. Your doctor must also test your blood before starting treatment with Moderiba. 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 Moderiba, 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 Moderiba 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 behaviour, 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 Moderiba 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 Moderiba

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 Moderiba 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 Moderiba 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 Moderiba. In addition, patients receiving zidovudine in combination with Moderiba and alfa interferons are at increased risk of developing anaemia.

Co-administration of Moderiba 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 Moderiba and peginterferon are at increased risk of developing severe blood disorders.

Please also read the package leaflets of the other medicines that are used in combination with Moderiba. 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.

Moderiba with food and drink

Moderiba 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.

Moderiba 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. Moderiba 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 Moderiba, 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 Moderiba, please see the section 'If you are a **man**'.

If you are a **man** who is taking Moderiba, 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 Moderiba.

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

Please also read the package leaflets of the other medicines that are used in combination with Moderiba for the treatment of hepatitis C.

Driving and using machines

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

Moderiba contains lactose

If you have been told by your doctor that you have an intolerance to some sugars, contact your doctor before taking this medicine.

3. How to take Moderiba

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 Moderiba.

The recommended dose ranges between 800 mg to 1400 mg/day depending on the other medicines you are using in combination with Moderiba.

- - 800 mg/day: Take 400 mg in the morning and 400 mg in the evening
- - 1000 mg/day: Take 400 mg in the morning and 600 mg in the evening
- - 1200 mg/day: Take 600 mg in the morning and 600 mg in the evening
- - 1400 mg/day: Take 600 mg in the morning and 800 mg in the evening

In 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 Moderiba varies, depending on the type of virus you are infected with, which other medicine you are being treated with, 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 Moderiba.

If you have the impression that the effect of Moderiba 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.

Please also read the package leaflets of the other medicines that are used in combination with Moderiba.

If you take more Moderiba than you should

Contact your doctor or pharmacist as soon as possible.

If you forget to take Moderiba

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 Moderiba

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.

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.

Please also read the package leaflets of the other medicines that are used in combination with Moderiba for information on the side effects of those products.

The side effects listed in this section were observed primarily when Moderiba 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):

- 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 tract 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, pneumonia, 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 1,000 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 (cerebrovascular events)
- 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 characterized 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 (inflammation of the colon from decreased blood supply), ulcerative colitis (inflammatory disease of the colon), 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 Moderiba 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.

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 via HPRA Pharmacovigilance, Earlsfort Terrace, IRL - Dublin 2; Tel: +353 1 6764971; Fax: +353 1 6762517. Website: www.hpra.ie; e-mail: medsafety@hpra.ie. By reporting side effects you can help provide more information on the safety of this medicine.

5. How to store Moderiba

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

This medicine does not require any special temperature storage conditions. Keep the bottle tightly closed in order to protect from moisture.

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 Moderiba contains

- Each film-coated tablet contains 200, 400 or 600 mg of the active substance ribavirin.
- The other ingredients are microcrystalline cellulose, lactose monohydrate, croscarmellose sodium, Povidone and magnesium stearate.
- The film coating contains polyvinyl alcohol, titanium dioxide (E171), Macrogol 3350, talc, indigotine aluminium lake (E132) (200 mg), Brilliant Blue FCF aluminium lake (E133) (400 mg and 600 mg) and Carnauba wax.

What Moderiba look like and contents of the pack

Moderiba tablets are unscored blue capsule-shaped film-coated tablets, with dimensions of 12.0 mm x 6.0 mm (200 mg), 17.5 mm x 7.0 mm (400 mg) or 18.6 mm x 7.6 mm (600 mg), marked with '3RP' on one side and with '200', '400' or '600' on the other. Moderiba tablets are packed into bottles containing 168 tablets (for the 200 mg) or 56 tablets (for the 400 mg and 600 mg).

Not all pack sizes may be marketed.

Marketing Authorisation Holder and Manufacturer

Marketing Authorisation Holder
AbbVie Limited
Citywest Business Campus
Dublin 24
Ireland

Manufacturer:
AbbVie Deutschland GmbH & Co. KG
Knollstrasse
67061 Ludwigshafen
Germany

This medicinal product is authorised in the Member States of the EEA under the following names:

Austria, Germany	Moderiba 200/400/600 mg Filmtabletten
Belgium	Moderyba 200/400/600 mg Comprimés Pelliculés
Denmark	Moderiba Filmovertrukne Tabletter
Estonia	Moderiba 200/400/600 mg õhukese polümeerikattega tableted
Finland	Moderiba 200/400/600 mg kalvopäällysteiset tabletit
Hungary	Moderiba 200/400/600 mg filmtabletta
Ireland	Moderiba 200/400/600 mg film-coated tablets
Italy	Moderiba 200/400/600 mg compresse rivestite con film
Latvia	Moderiba 200/400/600 mg Apvalkotās Tabletes
Lithuania	Moderiba 200/400/600 mg plėvele dengtos tabletės
Poland	Moderiba 200/400/600 mg tabletki powlekane
Sweden	Moderiba 200/400/600 mg filmdragerad tablett

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