EMA/681255/2015
EMEA/H/C/000246

EPAR summary for the public

Rebetol

ribavirin

This is a summary of the European public assessment report (EPAR) for Rebetol. It explains how the Committee for Medicinal Products for Human Use (CHMP) assessed the medicine to reach its opinion in favour of granting a marketing authorisation and its recommendations on the conditions of use for Rebetol.

What is Rebetol?

Rebetol is a medicine that contains the active substance ribavirin. It is available as capsules (200 mg) and as an oral solution (40 mg/ml).

What is Rebetol used for?

Rebetol is used in combination with other medicines to treat adults with long-term hepatitis C (a disease of the liver due to infection with the hepatitis C virus). It can also be used in previously untreated patients aged three years and over whose livers are working properly.

The medicine can only be obtained with a prescription.

How is Rebetol used?

Treatment with Rebetol should be started and monitored by a doctor who has experience in the management of long-term hepatitis C.

The dose of Rebetol is based on the patient's body weight, and ranges from five to six capsules a day in adults. In children weighing between 47 and 65 kg the dose ranges from 3 to 4 capsules. Children above 3 years of age and adolescents who weigh less than 47 kg or who cannot swallow capsules should take the oral solution at a dose of 15 mg per kilogram body weight a day. Rebetol is taken with food each day in two divided doses (morning and evening). The duration of treatment depends on the patient's condition and response to treatment, and ranges from six months to a year. The dose may

30 Churchill Place ● Canary Wharf ● London E14 5EU ● United Kingdom
Telephone +44 (0)20 3660 6000 **Facsimile** +44 (0)20 3660 5555
Send a question via our website www.ema.europa.eu/contact

need to be adjusted for patients who experience side effects. For more information, see the package leaflet.

How does Rebetol work?

The active substance in Rebetol, ribavirin, is an antiviral belonging to the class 'nucleoside analogues'. Rebetol is thought to interfere with the production or action of viral DNA and RNA, which are needed for viruses to survive and multiply. Rebetol on its own has no effect on eliminating the hepatitis C virus from the body.

How has Rebetol been studied?

Rebetol has been studied in a total of over 6,000 adults who had not been treated before, including 328 patients with cirrhosis and 507 patients also infected with HIV. It has also been studied in 1,699 adults whose disease had come back after previous treatment or whose previous treatment had failed. Rebetol has also been studied in 177 children and adolescents aged between three and 17 years who had not been treated before. In all of the studies, Rebetol was given in combination with interferon alfa-2b or peginterferon alfa-2b. In most of the studies, the main measure of effectiveness was the amount of virus in the blood before and after six months or a year of treatment, and at 'follow-up', six months later. Some studies also looked at signs of improvement of the condition of the liver.

Two main studies involving 1,503 adult patients with type 1 hepatitis C and compensated liver disease investigated the effect of ribavirin in a triple therapy combination with peginterferon alfa-2b and boceprevir. The main measure of effectiveness in these studies was the number of patients who had no detectable hepatitis C virus in their blood 24 weeks after the end of the treatment and could therefore be considered to be cured.

Additional data from the published literature show the positive effects of ribavirin-containing medicines when taken in different combinations, including combinations with peginterferon alfa-2a and a class of medicines known as direct acting antivirals (or DAAs).

What benefit has Rebetol shown during the studies?

In adults who had not been treated before, Rebetol in combination with interferon alfa 2b was more effective than interferon alfa 2b on its own, with 41% of the patients responding to the combination treatment and 16% to the interferon alone. Response rates were higher when Rebetol was used with peginterferon alfa 2b. Rebetol in combination with peginterferon alfa 2b was also effective in adults with cirrhosis or HIV. Combination treatment including Rebetol was effective in around a quarter of the adults whose disease had come back after previous treatment or whose previous treatment did not work, and over half of the children and adolescents treated.

In the studies on triple therapy in patients with type 1 hepatitis C and compensated liver disease, ribavirin in combination with peginterferon alfa 2b and boceprevir was shown to be more effective than the dual combination with peginterferon alfa 2b alone. Triple therapy led to a 30% increase in the number of previously untreated early responders who were cured after six months. A 40% increase was seen among patients who had been treated before.

What is the risk associated with Rebetol?

Haemolytic anaemia (anaemia caused by abnormal breakdown of red blood cells) is a common side effect (seen in between 1 and 10 patients in 100), usually during the first few weeks of treatment. The haemolytic anaemia may affect a patient's heart function and lead to abnormal test values for substances such as uric acid and bilirubin in the blood. There are several other side effects of Rebetol, some of which are very common (occurring in more than 1 in 10 patients). For the full list of side effects reported with Rebetol, see the package leaflet.

Rebetol must not be used in patients with severe heart disease and blood disorders such as thalassaemia and sickle cell anaemia or in pregnant or breast-feeding women. For a full list of restrictions, see the package leaflet.

Why has Rebetol been approved?

The CHMP decided that Rebetol's benefits are greater than its risks and recommended that it be given marketing authorisation.

The Committee noted that Rebetol in combination with other medicines, including peginterferon alfa and DAAs is effective against long-term hepatitis C virus infection in adults and children.

What measures are being taken to ensure the safe and effective use of Rebetol?

A risk management plan has been developed to ensure that Rebetol is used as safely as possible. Based on this plan, safety information has been included in the summary of product characteristics and the package leaflet for Rebetol, including the appropriate precautions to be followed by healthcare professionals and patients.

Other information about Rebetol

The European Commission granted a marketing authorisation valid throughout the European Union for Rebetol on 7 May 1999.

The full EPAR for Rebetol can be found on the Agency's website: ema.europa.eu/Find medicine/Human medicines/European public assessment reports. For more information about treatment with Rebetol, read the package leaflet (also part of the EPAR) or contact your doctor or pharmacist.

This summary was last updated in 10-2015.