Copeg

Ribavirin 200 mg

COMPOSITION
Each capsule contains Ribavirin BP 200 mg.

PHARMACOLOGICAL INFORMATION
Therapeutic class: Antiviral agent

PHARMACOLOGICAL ACTION

Description
Ribavirin is an anti-viral drug indicated for severe RSV infection (individually), Hepatitis C infection (used in conjunction with Peginterferon) and other viral infections. Ribavirin is a prodrug, which when metabolised resembles purine RNA nucleotides. In this form it interferes with RNA metabolism required for viral replication. How it exactly affects viral replication is unknown; many mechanisms have been proposed for this but none of these has been proven to date. Multiple mechanisms may be responsible for its actions.

Mechanism of Action
Ribavirin is a synthetic nucleoside analogue that has shown in vitro activity against some RNA and DNA viruses. Oral formulations of Ribavirin monotherapy have been investigated as therapy for chronic Hepatitis C in several clinical trials. Results of these investigations showed that Ribavirin monotherapy had no effect on eliminating Hepatitis virus (HCV-RNA) or improving hepatic histology after 6 to 12 months of therapy and 6 months of follow-up. However, clinical trials combining Ribavirin with Peginterferon or interferon resulted in an increased response rate over treatment with pegylated interferon or interferon alone. The mechanism by which Ribavirin in combination with Peginterferon or interferon exerts its effects against HCV is unknown.

CLINICAL INFORMATION

Therapeutic Indications
Ribavirin is indicated in combination with peg-interferon alpha-2a, 2b or interferon alpha injection for the treatment of chronic Hepatitis C in patients with compensated liver disease previously untreated with alpha interferon or who have relapsed following alpha interferon therapy. Patients in whom efficacy was demonstrated included patients with compensated liver disease and histological evidence of cirrhosis.

Dosage
Ribavirin Capsules must not be used alone because Ribavirin is not effective as monotherapy in the treatment of Hepatitis C.

Ribavirin must be used in combination with either Peginterferon or interferon. The choice of combination regimen is based on the characteristics of the patient.

Ribavirin Capsules in combination with Peginterferon solution
The dose of Ribavirin is based on patient body weight. Ribavirin capsules are to be administered orally each day in two divided doses with food (morning and evening).

Ribavirin doses (in combination with Peginterferon)

Ribavirin dose based on body weight

Patient weight (kg)	Daily Ribavirin dose	Number of 200 mg capsules
< 65	800 mg	4 (2 morning + 2 evening)
65 – 85	1,000 mg	5 (2 morning + 3 evening)
> 85	1,200 mg	6 (3 morning + 3 evening)

Duration of treatment
Predictability of sustained virological response: Patients infected with virus genotype 1 who fail to achieve virological response at Week 12 are highly unlikely to become sustained virological responders.

- Genotype 1: For patients who exhibit virological response at week 12, treatment should be continued for another nine month period (i.e., a total of 48 weeks). In the subset of patients with genotype 1 infection and low viral load (<2,000,000 copies/mL) who became HCV RNA negative at treatment week 4 and remain HCV RNA negative at week 24, the treatment could either be stopped after this 24 week treatment course or pursed for an additional 24 weeks (i.e. overall 48 weeks treatment duration). However, overall 24 weeks treatment duration may be associated with a higher risk of relapse than 48 weeks treatment duration.
- Genotypes 2 or 3: It is recommended that all patients be treated for 24 weeks.
- Genotype 4: In general, patients infected with genotype 4 are considered harder to treat and limited study data (n=66) indicate they are compatible with a duration of treatment as for genotype 1.

Ribavirin Capsules in combination with interferon solution
Ribavirin Capsules are administered orally at a dose of 1000 mg or 1200 mg daily in two divided doses (morning and evening), in combination with interferon solution for Injection administered subcutaneously at a dose of 3 million IU three times a week (every other day).

The recommended dose of RIBAVIRIN Capsules in combination with interferon depends on the patient's body weight:
Patients weighing <75 kg should receive 1000 mg daily as two 200 mg capsules in the morning and three 200 mg capsules in the evening.

Patients weighing >75 kg should receive 1200 mg daily as three 200 mg capsules in the morning and three 200 mg capsules in the evening.

Duration of treatment

Predictability of sustained virological response
The recommended duration of treatment is up to 1 year. Duration should be individualized in accordance with the baseline characteristics of the disease, response to therapy and tolerance of the regimen. After 6 months of treatment, virologic response should be assessed. If virologic response has not been achieved by 6 months, discontinuation of Ribavirin in combination with Peginterferon or interferon solution should be considered.

- Genotype 1: Treatment should be continued for another six months period (i.e., a total of one year) in patients who exhibit negative HCV-RNA after six months of treatment.
- Genotypes Non-1: The decision to extend therapy to one year in patients with negative HCV-RNA after six months of treatment should be based on other prognostic factors (e.g., age > 40 years, male gender, bridging fibrosis).

Side Effects
Nausea, vomiting, headache, dizziness, blurred vision, stomach upset, trouble sleeping, and flu-like symptoms (e.g. fever, chills, sore throat, muscle aches) may occur. Other severe side effects include hair loss, loss of appetite, weight loss, rash, itching, fatigue, dark urine, yellowing of eyes, mood changes (including severe depression or suicidal thoughts), trouble breathing, chest pain, muscle pain, joint pain, rapid breathing, stomach pain, easy bruising or unusual bleeding.

Contraindications: Ribavirin is contraindicated in patients with known hypersensitivity to Ribavirin or any components of the capsule, women who are pregnant, men whose female partners are pregnant, patients with hemoglobinopathies (e.g. thalassemia major or sickle cell anemia), autoimmune Hepatitis or hepatic decompensation before or during treatment. No pharmacokinetic interactions were noted between peg-interferon alpha and Ribavirin.

Precautions: Before using this medicine, consult your doctor if you have: severe heart disease, kidney disease, blood disorders (e.g. sickle cell anemia, low hemoglobin), other types of Hepatitis (e.g. autoimmune Hepatitis), other liver problems, heart problems, breathing problems, pancreas problems (e.g. pancreatitis), diabetes, any allergies. Use caution engaging in activities requiring alertness such as driving or using machinery. Caution is advised when using this drug in the elderly because they may be more sensitive to its effects.

Pregnancy and lactation: This medication must not be used during pregnancy. It is not known whether this drug passes into breast milk. Because of the potential risk to the infant, breast-feeding while using this drug is not recommended.

PHARMACEUTICAL INFORMATION

Storage conditions
Store in a cool and dry place, away from light. Keep out of the reach of children.

Packaging
Copeg Capsule: Each commercial box contains 2 x 10's capsules in Alu-PVDC blister pack.

Manufactured By
BEACON Pharmaceuticals Limited
Mymensingh, Bangladesh

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