Ribavirin (Copegus, Rebetol, Ribasphere)

Drug Summary

Ribavirin has been an integral component of hepatitis C therapy. The use of ribavirin with interferon or peginterferon for the treatment of hepatitis C is no longer recommended due to the poor efficacy and high rate of adverse effects with this regimen. Currently, still plays a role on a limited basis in combination with some direct-acting antiviral agents and combinations. Dosing of ribavirin is somewhat complicated and includes fixed-dose and weight-based ribavirin, with dosing depending on the genotype and brand of ribavirin used. In addition, ribavirin can cause severe anemia and dose adjustment is required in some patients who develop anemia.

Class and Mechanism

Ribavirin is a purine nucleoside analog that has an incompletely understood mechanism of action against hepatitis C virus. Investigators have proposed four main potential sites of ribavirin action against hepatitis C virus: (1) augmentation of host T-cell immune clearance of HCV, (2) inhibition of the host enzyme inosine monophosphate dehydrogenase (IMPDH) that results in depleted pools of guanosine triphosphate, an essential substrate for viral RNA synthesis (3) direct inhibition of HCV replication, and (4) induction of RNA virus mutagenesis that drives HCV to an abnormally high error rate.

Manufacturer for United States

Ribavirin is manufactured by multiple companies in the United States: Copegus (Figure 1) is produced by Genentech (member of the Roche group), Rebetol by Merck Sharp & Dome, a subsidiary of Merck & Co., Inc., and Ribasphere by Kadmon Pharmaceuticals (originally by Three Rivers Pharmaceuticals which was acquired by Kadmon Pharmaceuticals). In addition, several companies, including Sandoz (Figure 3) and Teva (Figure 4) pharmaceuticals, produce generic ribavirin.
Cost and Medication Access

The wholesale acquisition cost (WAC) for ribavirin is difficult to report, given the multiple brand and generic preparation and given the variable doses used with weight-based dosing. In general, the generic preparations are less expensive than the brand drugs. As a rough estimate, a 12-week course of generic ribavirin is in the range of $550 to $850. Accordingly, the ribavirin component of a 48-week treatment course costs approximately $1100 to $1700.

Rebetol Patient Assistance: For information regarding reimbursement support services for ribavirin (Rebetol), see the ACT Program website or call 866-363-6379. This is the same patient assistance program for peginterferon alfa-2b (Pegintron).

Copegus Patient Assistance: For information regarding coverage, reimbursement, and patient assistance for Copegus, visit the Access Solutions website or call 888-941-3331. This is the same patient assistance program for peginterferon alfa-2a (Pegasys).

Ribosphere, RibapakPatient Assistance: For information regarding reimbursement support services for ribavirin (Rebetol), contact the Kadmon Enabling Your Success (K.E.Y.S.) Program at 888-668-3393.

Adverse Effects

Two potentially serious ribavirin-associated adverse effects are listed as black box warnings.

- Hemolytic Anemia: Ribavirin can cause a potentially severe hemolytic anemia. The hemolytic anemia can occur suddenly and can result in worsening of cardiac disease, even leading to myocardial infarction. The hemolytic anemia most often occurs within 1 to 2 weeks after starting therapy. Accordingly, patients should have a hematocrit and/or hemoglobin checked prior to starting therapy and at week 2 and 4 of therapy.
- Birth Defects: Ribavirin can cause significant teratogenic and embryocidal effects, including potential birth defects and fetal death. Ribavirin should not be used by women during pregnancy or in male partners of women who are pregnant. For women who will receive treatment with ribavirin, a documented negative pregnancy test is required immediately prior to starting ribavirin therapy and women should use two or more forms of birth control and have monthly pregnancy testing during treatment and for 6 months thereafter. Further, pregnancy should be avoided for at least 6 months after completing ribavirin therapy (for females who have taken ribavirin and for females partners of males who have taken ribavirin).

Other less serious adverse effects have been observed with ribavirin, including fatigue, nausea, rash, and itching. To report suspected adverse reactions, contact (1) the ribavirin manufacturer or (2) the FDA at 1-800-FDA-1088.

Key Drug Interactions

For complete information on ribavirin-related drug interactions, see the Drug Interactions section in
the Ribavirin (Copegus, Rebetol, Ribasphere) Prescribing Information.

The most up to date version of this content may be obtained from: https://www.hepatitisc.uw.edu/page/treatment/drugs/ribavirin-drug