

Indiana Medicaid Therapeutics Committee Therapeutic Class Review Summary

Therapeutic class:

Agents to Treat Hepatitis C

Overview:

Hepatitis C is a contagious, blood-borne viral infection that could lead to inflammation or permanent damage of the liver. According to the U.S. Centers for Disease Control and Prevention, 3.9 million Americans have been infected with HCV, of which 2.7 million are chronically infected. About 35,000 new cases of hepatitis C are estimated to occur in the United States each year. It is also estimated that the annual U.S. healthcare cost for HCV will exceed \$1 billion by the year 2008 and continue to increase until at least the year 2015. HCV infections begin with a sudden (acute) illness, often so mild that people do not notice symptoms. If symptoms do develop, they may include: fatigue, malaise, and mild abdominal pain. About 85% of people with the acute illness will go on to develop long-term (chronic) infection. Chronic hepatitis C usually progresses at a very slow rate, often over a period of 10 to 30 years. However, more damage occurs to the liver the longer the virus is in the body. If the disease remains untreated, serious consequences such as cirrhosis, liver failure, liver cancer, or even death may occur.

There is no vaccine to prevent hepatitis C. However, the advances in medical therapy now provide the possibility to clear HCV in many patients. These antiviral agents include interferon alfa-2a, peginterferon alfa-2a, interferon alfa-2b, peginterferon alfa-2b, interferon alfacon-1, and ribavirin. Interferons are a family of proteins produced by nucleated cells that have antiviral, antiproliferative, and immune-regulating activity. They exert antiviral effects by augmenting the production and/or release of specific enzymes, which contribute to inhibition of viral replication. The general concerns of interferons are depression, fatigue and flu-like symptoms. Pegylated interferons are conjugated interferons, which have higher molecular weight and longer half-life. The mechanism of action and adverse effect profiles are similar to interferons. Ribavirin is an oral antiviral agent that has activity against a broad range of viruses. As monotherapy, ribavirin has little effect on HCV, but adding it to interferon increases the sustained response rate by two to three fold. Ribavirin is marketed as Rebetol[®] to use in combination with interferon alfa-2b and Copegus[™] to use in combination with interferon alfa-2a. The major adverse events associated with ribavirin are anemia, fatigue, and irritability.

In general, pegylated interferons (PEG-Intron[®] and Pegasys[®]) are more effective than interferons (Intron[®]-A and Roferon[®]-A) and combination therapies with ribavirin are more effective than monotherapy. Evidence has shown that after 48 weeks of treatment with peginterferon alfa-2b, between 18% and 23% (depending on the dose) of patients had no evidence of the virus in their blood, compared with 12% of patients taking standard interferon. In a randomized study, a significantly higher proportion of patients who received peginterferon alfa-2a plus ribavirin had a sustained virologic response 24 weeks after cessation of therapy than patients who received interferon alfa-2b plus

ribavirin (56% and 44%, respectively) or peginterferon alfa-2a alone (29%). Combination treatment with standard interferon and ribavirin generally stops the virus in about 40% of patients; of those who take interferon alone, about 16% achieve good, long-term control of the virus. In patients who have never responded to interferon alone, standard interferon and ribavirin stop the virus in up to 20% of patients.

Generic Name	Brand Name	Manufacturer
Peginterferon Alfa-2a	Pegasys [®]	Roche
Peginterferon Alfa-2b	PEG-Intron [®]	Schering Corporation
Ribavirin	Rebetol [®] , Copegus [™]	Schering Corporation, Roche, various

Summary:

Ribavirin is an oral antiviral agent that has activity against a broad range of viruses. As monotherapy, ribavirin has little effect on HCV, but adding it to interferon increases the sustained response rate significantly. In general, pegylated interferons are more effective than interferons and combination therapies with ribavirin are more effective than monotherapy. The preferred drug list should be based upon FDA-approved indications, efficacy, adverse effects, and cost.