

# Pegasys Granted Priority Review

*Liz Highleyman*



[Print this page](#)

On July 15, the U.S. Food and Drug Administration (FDA) put Pegasys—Hoffman-La Roche's brand of pegylated interferon in combination with Roche's ribavirin—on its agenda for a priority review approval. Under the six-month priority designation, the FDA is expected to review and make a decision about Roche's New Drug Application for Pegasys in combination with ribavirin (submitted in June) by the end of the year. Pegasys monotherapy and combination therapy was approved by the European Commission—the European Union's counterpart to the FDA—in June and is already available in many countries in Latin America and Asia.

The FDA's priority designation is intended for therapies that address unmet medical needs, offering an improvement in the safety or effectiveness of treatments currently available.

Interferon is a genetically engineered version of a protein produced by the immune system. It stimulates immune function and has an antiviral effect. Pegylated interferon is a chemically altered version of standard interferon in which a polyethylene glycol molecule is added to extend the life of the drug within the body. This allows pegylated interferon to be injected once per week, instead of the three times per week recommended for standard interferon. Pegasys is a pegylated form of interferon-alpha 2a. Schering-Plough's Peg-Intron—which has been on the market for a year and a half—is a pegylated version of interferon-alpha 2b.

Pegasys is a ready-to-use solution that is injected under the skin. In contrast, Peg-Intron comes as a powder that must be reconstituted before use. Pegasys is given at a standard dose (unlike Peg-Intron, which is dosed by body weight). Peg-Intron in combination with ribavirin was approved for one-year treatment duration for all genotypes of HCV. Roche is seeking approval for 12-month Pegasys combination treatment duration for genotype 1 and six-month treatment duration for genotypes 2 and 3.

Studies have shown that combination therapy with pegylated interferon plus ribavirin is more effective than treatment with standard interferon plus ribavirin, especially in patients with genotype 1. The recently revised National Institutes of Health draft consensus statement on management of hepatitis C recommends combination therapy with pegylated interferon plus ribavirin as the most effective treatment for chronic HCV.

At the European Association for the Study of the Liver conference in April 2002, researchers presented much-anticipated data on Pegasys in combination with ribavirin. The Roche Global 942 Phase III multi-national study, which compared combination treatment with Pegasys to combination therapy with standard interferon, included over 1,200 participants. Using an intent-to-treat analysis, patients who received Pegasys obtained the highest sustained virological response rate (SVR, undetectable HCV viral load six months after the end of therapy) seen to date—61% overall. Breaking this down, SVR was achieved in 51% of those with genotype 1, 78% of those with non-1 genotypes, 50% of those with liver cirrhosis, and 65% of those without cirrhosis. In addition, a study reported at the May 2002 Digestive Disease Week conference showed that 54% of participants receiving Pegasys demonstrated improved liver histology (reversal of tissue damage from one biopsy to the next) compared to 31% of those receiving standard interferon.

In its application for Pegasys combination approval, Roche cited two large studies that included over 2,400 patients. According to the company, the safety and effectiveness of Pegasys has been studied in nearly 20,000 persons overall, including difficult-to-treat patients such as those with HIV/HCV coinfection, African-Americans, post-transplant patients,

and those with decompensated cirrhosis or kidney disease. Roche has applied for approval of Pegasys for HCV positive people including those with compensated cirrhosis; interferon treatment is potentially dangerous for people with decompensated cirrhosis (end-stage liver disease), and such people should be treated in clinical trials. The NIH recently selected Pegasys rather than Peg-Intron for use in the HALT-C trial, which will study the role of long-term interferon maintenance therapy in 900 patients who failed to respond to previous HCV therapy.

Side effects of Pegasys combination therapy in the two clinical trials cited in the application were less than seen with standard interferon combination therapy. In contrast, studies of Peg-Intron combination therapy demonstrated greater side effects than standard interferon combination therapy in Schering-Plough's pivotal trial. The most common side effects of Pegasys include flu-like symptoms, fever, fatigue, headache, nausea, diarrhea, loss of appetite, partial hair loss, muscle and joint aches, and pain at the injection site. Potentially more serious adverse effects include low white blood cell counts due to bone marrow suppression—which can raise the risk of infections—and mental symptoms such as irritability and depression.

To date, Pegasys and Peg-Intron have not been directly compared in head-to-head trials. In clinical studies comparing pegylated interferon with standard interferon, combination therapy using Pegasys appears to have an overall effectiveness similar to combination therapy using Peg-Intron in terms of achieving a sustained virologic response. However, studies of Pegasys have shown more effectiveness in treating people with genotype 1, including those with a high viral load and patients with cirrhosis—the most difficult patients to treat. There also is evidence that Pegasys may be more easily tolerated and have fewer side effects than Peg-Intron.

While it remains to be seen which version of pegylated interferon is better, patients certainly will benefit by having another treatment option available once the FDA approves Pegasys.