

Peginterferon alfa-2a (*Pegasys*)

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Drug Summary

Peginterferon alfa-2a has been the cornerstone of treatment for chronic hepatitis C since its introduction as an improved alternative to standard interferon alfa more than a decade ago. In 2014, peginterferon alfa-2a continues to play an important role in the treatment of hepatitis C. Most importantly, the combination of peginterferon alfa plus ribavirin plus sofosbuvir is currently the preferred regimen for patients with genotypes 1 and 4, with peginterferon alfa plus ribavirin plus simeprevir an alternative. Regimens with peginterferon alfa that are no longer considered preferred are (a) peginterferon alfa plus ribavirin plus either boceprevir or telaprevir for genotype 1 or (b) peginterferon alfa plus ribavirin for genotype 2 or 3. Although peginterferon alfa-2a is expensive, it is significantly less expensive than direct acting antiviral agents, especially sofosbuvir and simeprevir. In addition, enthusiasm for peginterferon alfa-2a has been hindered by its extensive adverse effects, necessity for weekly injections, and limited efficacy in certain patient populations, including those patients who are cirrhotic, HIV-coinfected, or who carry the IL28B TT genotype. In the future, it is likely that peginterferon alfa will become obsolete as numerous interferon-free combination regimens become available and eventually become recommended for all hepatitis C genotypes.

Class and Mechanism

Peginterferon alfa-2a consists of interferon alfa-2a covalently linked to a 40-kd branched polyethylene glycol (PEG). The biologic activity of peginterferon-alfa-2a derives from its interferon alfa-2a moiety, which impacts both adaptive and innate immune responses against hepatitis C virus. This alpha interferon binds to and activates human type 1 interferon receptors on hepatocytes which activates multiple intracellular signal transduction pathways, culminating in the expression of interferon-stimulated genes that produce an array of antiviral effects, such as blocking viral protein synthesis and inducing viral RNA mutagenesis. Compared with the native interferon alfa-2a, the peginterferon alfa-2a has sustained absorption, delayed clearance, and a prolonged half life.

Manufacturer for United States

Peginterferon alfa-2a is manufactured in the United States as *Pegasys* by Genentech ([Figure 1](#)), a member of the Roche Group.

Cost and Medication Access

The estimated wholesale acquisition cost (WAC) for peginterferon alfa-2a is approximately \$770 per 180 mcg dose. This corresponds to a cost of approximately \$9,250 for a 12-week supply, \$18,500 for a 24-week supply, and \$37,000 for a 48-week supply. For information regarding coverage, reimbursement, and patient assistance for peginterferon alfa-2a (*Pegasys*), visit the [Access Solutions](#) website or call 1-888-941-3331. This is the same patient assistance program for the Genentech manufactured ribavirin (*Copegus*).

Adverse Effects

In most patients, peginterferon alfa-2a causes numerous problematic side effects. In clinical studies involving peginterferon alfa-2a, the following adverse effects were reported most often: headache, fatigue, and influenza-like symptoms, including myalgia, pyrexia, arthralgia, nausea, and anorexia. In addition, significant hematologic toxicity can occur due to peginterferon alfa-2a, including neutropenia and thrombocytopenia. Patients can develop ophthalmologic disorders and all patients should receive a baseline eye examination and should have a prompt eye examination if they develop ocular symptoms. Neuropsychiatric effects such as insomnia, depression, and irritability can also occur. Peginterferon alfa-2a may cause or aggravate life-threatening neuropsychiatric, autoimmune, ischemic, or infectious disorders. Further, the use of peginterferon in patients with cirrhosis can cause life-threatening hepatic decompensation. To report suspected adverse reactions, contact (1) Genentech at 1-888-835-2555 or (2) the FDA at 1-800-FDA-1088.

Key Drug Interactions

There are few if any clinically significant drug interactions associated with the use of peginterferon alfa-2a. No effect on the pharmacokinetics of representative drugs metabolized by the cytochrome P450 system have been noted except for the inhibition of P450 1A2 enzyme, a 25% increase in theophylline AUC, and a 10% increase in methadone AUC. Serum levels of theophylline should be monitored in patients concomitantly receiving peginterferon alfa-2a and appropriate dose adjustments made when these drugs are used together. For patients receiving peginterferon alfa-2a and methadone, monitoring for signs and symptoms of methadone toxicity is recommended. For complete information on peginterferon alfa-2a-related drug interactions, see the [Drug Interactions section in the Peginterferon alfa-2a \(*Pegasys*\) Prescribing Information](#).

Figures

Figure 1 Packaging - Peginterferon alfa-2a (Pegasys)

Photo: Andrew Karpenko, University of Washington



Figure 2 Single Use Syringe - Peginterferon alfa-2a (Pegasys)

Photo: Andrew Karpenko, University of Washington



Figure 3 180 mcg/0.5 ml autoinjector - Peginterferon alfa-2a (Pegasys)

Photo: Andrew Karpenko, University of Washington



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