var drug_url = "peginterferon-alfa-drug";

Peginterferon alfa-2a *(Pegasys)*

See also
Peginterferon alfa-2b
.

Table of Contents

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 pus sofosbuvir is currently the preferred regimen for patients with genotypes 1 and 4, with peginterferon alfa plus ribavirin pus 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 signifcantly less expensive than direct acting antiviral agents, especially sofosbuvir and simeprevir. In addition, enthuasiasm 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 correspondes 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 Genetech 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) Genetech at 1-888-835-2555 or (2) the FDA at 1-800-FDA-1088.

Key Drug Interactions

For complete information on peginterferon alfa-2a-related drug interactions, see the Drug Interactions section in the Peginterferon alfa-2a (*Pegasys*) Prescribing Information.

Clinical Trials

Filter by Category

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- Resistance/Virological Failure
- Resistance/Virological Failure
- Resistance/Virological Failure
- Resistance/Virological Failure
- Pharmacology
- Pharmacology

AIDS Clinical Trials Group A5071 Study

In this phase 2 trial involving patients coinfected with HCV and HIV, investigators randomized 133 subjects to receive a 48-week treatment course with either peginteferon alfa-2a plus ribavirin or standard interferon alfa-2a plus ribavirin. The ribavirin, was administered in both arms as a gradual dose escalation of 600 mg/day for 4 weeks, 800 mg/day for 4 weeks, and then 1000 mg/day thereafter. Among study participants, 86% were on antiretroviral therapy and 10% had cirrhosis. Treatment with peginteferon alfa-2a was associated with higher SVR rate than with standard interferon alfa-2a (27% versus 12%, p=0.03). Premature discontinuation occurred in 12% of patients in each arm. This study clearly established that peginteferon alfa-2a and ribavirin was superior to standard interferon alfa-2a and ribavirin in persons coinfected with HCV and HIV.

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APRICOT Study

The phase 3, randomized, controlled APRICOT study is one of the sentinel trials of peginterferon alfa-2a in patients coinfected with HCV and HIV. Investigators randomized 868 HCV-HIV coinfected patients to one of three treatment arms, each 48 weeks in duration: (1) peginterferon alfa-2a plus ribavirin 800 mg/day, (2) peginterferon alfa-2a plus placebo, and (3) standard interferon alfa-2a plus

ribavirin 800 mg/day. Among study participants, 84% were on antiretroviral therapy and 16% had cirrhosis. The combination of peginterferon alfa-2a and ribavirin generated significantly higher sustained virologic response rates compared with peginterferon alfa-2a monotherapy (40% versus 20%, p<0.001) and standard interferon alfa-2a plus ribavirin (40% versus 12%, p<0.001). The difference in SVR rates was most notable in patients with genotype 1 infection (29% versus 14% and 7% respectively, p<0.001). In addition, patients in the standard interferon arm had higher treatment discontinuation rates than patients in the peginterferon alfa-2a arms. This study clearly established that (1) peginteferon alfa-2a and ribavirin was superior to standard interferon alfa-2a and ribavirin in persons coinfected with HIV, and (2) the addition of ribavirin to peginterferon alfa-2a significantly improves SVR rates in persons coinfected with HIV.

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Duration and Dose-Finding Study of Peginterferon alfa-2a and Ribavirin

This multicenter, phase 3, randomized, double-blind trial used a 2 x 2 factorial design to examine the efficacy of 24 versus 48 weeks of peginterferon alfa-2a plus ribavirin, as well as the difference between fixed low dose (800 mg/day) versus weight-based (1000 or 1200 mg/day) dosing of ribavirin in patients with chronic HCV infection. Investigators enrolled 1311 patients, among whom 740 had genotype 1 infection. In patients with genotype 1, significantly higher SVR24 rates were observed with weight-based ribavirin dosing (compared with fixed low dose ribavirin) and with 48 versus 24 weeks of therapy. Among patients with genotypes 2 or 3 infection, ribavirin dosing and duration of therapy did not significantly affect SVR rates. This study clearly demonstrated that treatment of genotype 1 HCV with peginterferon alfa-2a plus ribavirin generates significantly higher SVR24 rates when higher doses of ribavirin are used and patients receive a longer treatment duration.

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IDEAL Study

The IDEAL Study is one of the largest trials of both forms of peginterferon alfa, designed as a head-to-head comparison of the two forms of peginterferon alfa (2a versus 2b) and to also compare two doses of peginterferon alfa-2b. Treatment-naïve patients with genotype 1 infection were randomly assigned to one of three treatment arms: (1) standard-dose (1.5 mcg/kg) peginteferon alfa-2b plus ribavirin (800-1400 mg/day), (2) low-dose (1 mcg/kg) peginteferon alfa-2b plus ribavirin (800-1400 mg/day), and (3) standard-dose (180 mcg) peginteferon alfa-2a plus ribavirin (1000-1200 mg/day). Patients who had an early virologic response had markedly higher SVR rates than those who do not achieve an early virologic response. The rates of sustained virologic responses and the incidence of adverse effects did not differ substantially across these regimens.

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Peginterferon alfa-2a +/- Ribavirin versus Interferon alfa-2b + Ribavirin

This randomized controlled trial examined the efficacy and safety of combination therapy with peginterferon alfa-2a plus ribavirin compared with peginterferon alfa-2a plus placebo (monotherapy) or standard interferon alfa-2a plus ribavirin. A total of 1,121 treatment-naïve patients with chronic hepatitis C were enrolled in the trial. Sustained virologic response (SVR) rate at 24 weeks post-treatment was greater among patients who received peginterferon alfa-2a plus ribavirin than with

either interferon alfa-2a plus ribavirin or peginterferon alfa-2a monotherapy (56% versus 44% and 29% respectively, p<0.001). Independent predictors of SVR in this study included genotypes other than genotype 1, age less than 40 years, and body weight of 75 kg or less. The overall side effect profiles were similar between the three treatment arms. This study clearly established that (1) peginteferon alfa-2a and ribavirin was superior to standard interferon alfa-2a and ribavirin, and (2) the addition of ribavirin to peginterferon alfa-2a significantly improves SVR rates.

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Peginterferon alfa-2a versus Interferon alfa-2a

In this open label, phase 3 trial, investigators randomized 531 hepatitis C treatment-naïve patients with chronic hepatitis C to recieve a 48-week treatment course with peginterferon alfa-2a or standard interferon alfa-2a. Approximately 62% of the patients enrolled in the trial had genotype 1 HCV. Compared with patients in the standard interferon alfa-2a arm, patients in the peginterferon alfa-2a arm had a higher end-of-treatment response (69% versus 28%, p=0.001) and higher sustained virologic response rates (39% versus 19%, p=0.001). The frequency and severity of adverse effects were similar between treatment groups, aside from a trend toward lower incidence of depression among patients who received peginterferon alfa-2a (16% versus 23% in the standard interferon arm). This trial clearly demonstrated the superiority of peginterferon alfa-2a over standard interferon alfa-2a.

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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

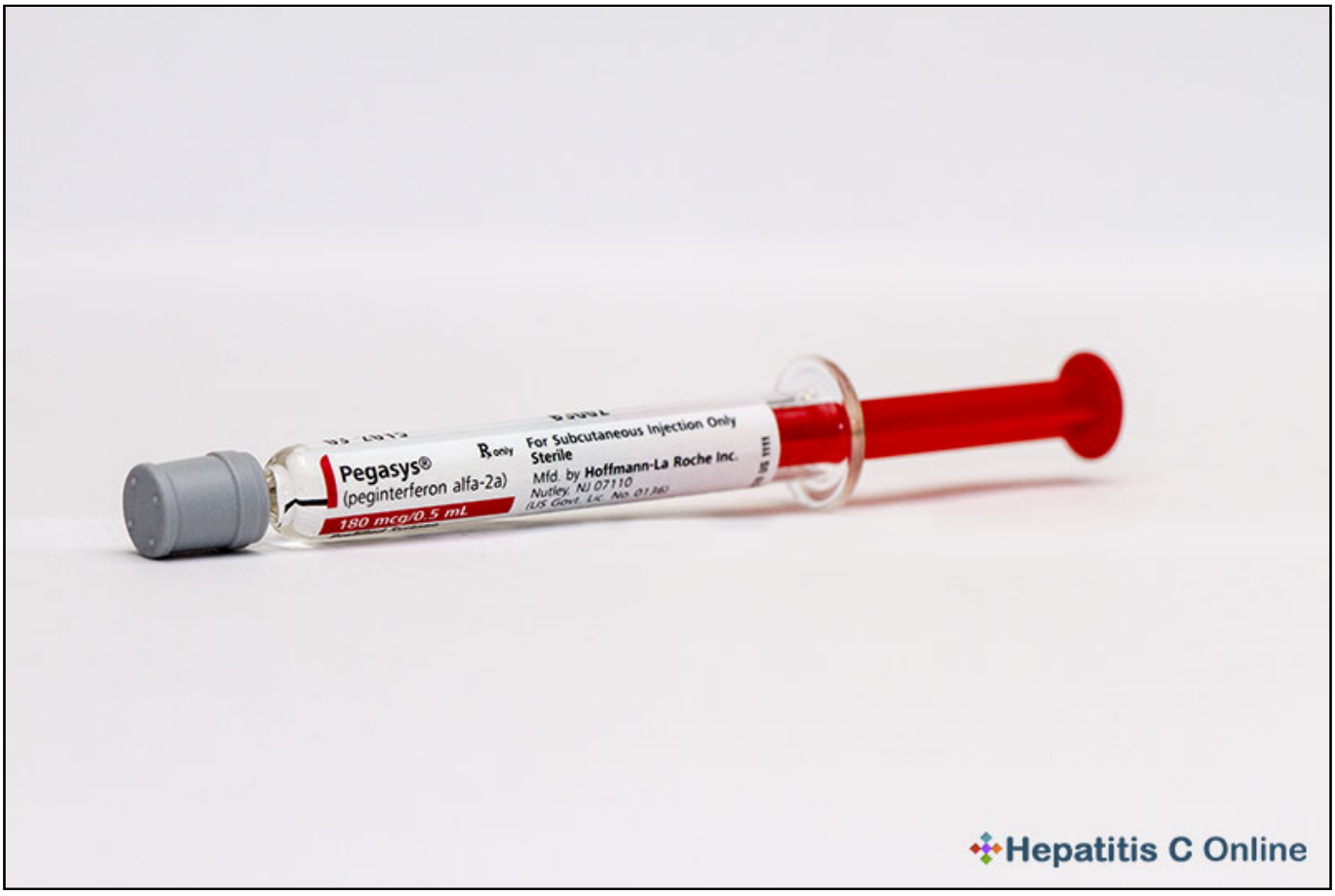

Figure 3 180 mcg/0.5 ml autoinjector - Peginterferon alfa-2a (Pegasys)

Photo: Andrew Karpenko, University of Washington