Pegasys medication guide
The FDA approval of Pegasys plus Copegus is based on the results from the APRICOT trial that was conducted in over 19 countries, including the United States. The study was a randomized, partially blinded study with three arms or study groups. This fact sheet will report on the information obtained from the FDA approved Pegasys plus Copegus medication guide and a follow-up study (PRESO) that used higher doses of ribavirin and a longer duration of treatment.

The patients in the APRICOT trial were randomized to receive standard interferon (interferon alfa-2a-Roferon-A) three times a week plus ribavirin 800 mg/day, or 180 mcg of Pegasys once weekly plus placebo, or 180 mcg of Pegasys once weekly with 800 mg/day of Copegus (ribavirin).

NOTE: It is important to note that the dose of ribavirin in both combination arms was 800 mg/day which is lower than the usual or standard dose used to treat people mono-infected with hepatitis C, genotype 1. This was due to concerns of possible increased anemia in HIV patients.
Eight hundred and sixty-eight adults were enrolled in this clinical trial. All trial participants had compensated liver disease, detectable hepatitis C virus, liver biopsy diagnosis of chronic hepatitis C and were previously untreated with interferon. In addition, patients also had a CD4+ cell count of greater than or equal to 200 cells/µL or a CD4+ cell count of greater than or equal to 100 cells/µL but less than 200 cells/µL and HIV-1-RNA less than 5000 copies/mL, and stable status of HIV. Approximately 15% of the patients in the study had cirrhosis.

The side effect profile in this study and listed in the indication was generally similar to that shown for HCV monoinfected patients in clinical trials of Pegasys plus Copegus. The side effects occurring more frequently in the coinfection study were neutropenia (40%), anemia (14%) thrombocytopenia (8%), weight decrease (16%), and mood alteration (9%).

One aspect of treating hepatitis C in someone with HIV/HCV is the potential for drug interactions between the HCV medications and the HIV medications and a couple of warnings are listed in the medication guide. There did not appear to be any pharmacokinetic or pharmacodynamic interactions when ribavirin was taken with lamivudine, stavudine, and/or zidovudine.

**Warning:** It is not recommended that didanosine (ddl) be taken at the same time as Pegasys plus Copegus. It was also noted that zidovudine (AZT) when taken with Pegasys plus Copegus could produce severe neutropenia and severe anemia more frequently than in similar patients not receiving zidovudine (neutropenia 15% vs. 9%), (anemia 5% vs. 1%).

**PRESCO**

When the APRICOT study was designed the dose for ribavirin was set at 800 mg for all genotype 1 patients regardless of weight. The suboptimal dosing schedule was due to the potential for drug interactions between ribavirin and HIV medications and the concern over ribavirin-induced anemia in HIV individuals who are already at higher risk for developing anemia.

Data from the PRESCO clinical trial of patients receiving Pegasys plus weight-based ribavirin (1,000/1,200 mg/day), were released in 2006 and confirmed that weight-based dosing of ribavirin is safe and more effective at the higher doses than the 800 mg dose in HIV and hepatitis C coinfected individuals.

**Results:** The study found that the sustained virological response (SVR) rates were 35.6% (genotype 1), 32.6% (genotype 4), and 72.4% (genotype 2 and 3).
**Pegasys plus Copegus**

**Extended Therapy**
PRESCo also included an arm that extended therapy to 72 weeks for genotype 1 patients and from 24 weeks to 48 weeks for genotype 2 and 3 patients.

**Results:** The extended duration SVR results for the genotype 1 and 4 group was 53% in the 72 week group compared to 31% in the 48 week group. In the genotype 2 and 3 group, 48 weeks of treatment resulted in an 82% SVR rate compared to a 67% SVR in the group that was treated for 24 weeks.

**Clinical Trials**
There are many clinical trials that include pegylated interferon, ribavirin and direct acting antivirals. For more information go to www.clinicaltrials.gov

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**Related publications:**

- **Incivek (telaprevir): 20 Grams of Fat**

- **Victrelis (boceprevir)**

- **Patient Assistance Programs**
  www.hcvadvocate.org/hepatitis/factsheets_pdf/Patient%20Assistance%20Programs.pdf

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**For more information**

- **American Association for the Study of Liver Diseases**
  www.aasld.org

- **Centers for Disease Control and Prevention**
  www.cdc.gov

- **Food and Drug Administration (FDA):**
  www.fda.gov

- **Mayo Clinic**
  www.mayoclinic.com

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