

## PEGASYS® and COPEGUS® Combination Therapy

### Quick Facts:

PEGASYS® (peginterferon alfa-2a (40KD)) plus COPEGUS® (ribavirin) is recommended as a first-line therapy for chronic hepatitis C.

PEGASYS is licensed to treat the broadest range of patients, including those with chronic hepatitis C, HIV-HCV co-infection, and chronic hepatitis B.

PEGASYS' unique branched-chain PEG means it stays in the body for the whole week between injections to fight the virus.

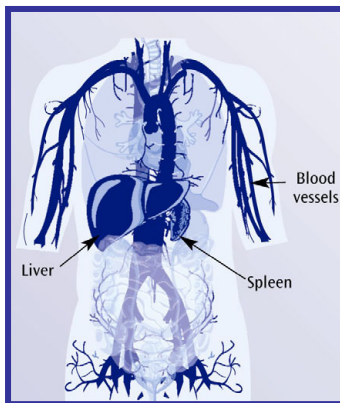
### What is PEGASYS?

PEGASYS is a modified form of interferon, a naturally occurring protein produced by the body to fight viruses.

PEGASYS is made by attaching a branched 40KD polyethylene glycol (PEG) chain to interferon alfa.

This allows the interferon to be absorbed more slowly and stay active in the body longer, so it can fight the virus for the full week between injections.

- The particular form of pegylation used in PEGASYS means that it is concentrated in the blood and targets tissues with a good blood supply, like the liver – the organ affected by HCV.
- It also means that one 180 µg dose of PEGASYS can be used without any need to change dose depending on a patient's weight.<sup>6</sup>



### What is COPEGUS?

COPEGUS is Roche's form of ribavirin, specifically developed for use with PEGASYS.

Ribavirin is an anti-viral drug that makes PEGASYS more effective in curing hepatitis C.

**Figure: PEGASYS is concentrated within the body in the blood and tissues with a good blood supply**

The chance of being cured of hepatitis C has never been better than it is today, thanks to the unsurpassed efficacy and safety of pegylated interferons like PEGASYS. Normally used in combination with COPEGUS, these products have advanced the treatment of this viral infection so that cure rates as high as 84% are now possible in certain patient populations.<sup>1</sup> Pegylated interferons are recommended as first-line therapy for chronic hepatitis C.<sup>2</sup>

### PEGASYS plus COPEGUS – Treating the Broadest Range of Patients

- PEGASYS has been studied in an unprecedented clinical trials programme that has ranged from pioneering studies in patients with cirrhosis to the first and only global trial in patients co-infected with HIV and HCV.
- To date, over 11,000 patients have been enrolled in Roche’s comprehensive clinical development programme, in addition to the numerous local clinical studies involving over 40,000 patients.

Roche’s continual investment in landmark clinical trials means that PEGASYS plus COPEGUS is licensed to treat the broadest range of patients, including those with:

### Chronic Hepatitis C

There are four common forms of the hepatitis C virus (HCV), called genotypes.

Genotype 1 is the most difficult-to-treat, and the most common, form of the virus.

- In clinical trials, 52% of patients with genotype 1 HCV were cured (also called a sustained virological response, or SVR) after taking PEGASYS 180 µg weekly plus COPEGUS 1,000-1,200 mg daily for 48 weeks.<sup>1</sup>

Genotypes 2 and 3 are considered easier-to-treat forms of the virus.

- Cure rates as high as 84% have been recorded with PEGASYS plus a low (800 mg daily) dose of COPEGUS.<sup>1</sup>
- Furthermore, these patients only need to be treated for 24 weeks.

Genotype 4 is common in the Middle East only.

- Cure rates as high as 69-79% have been reported in patients with genotype 4 HCV following 48 weeks of therapy with PEGASYS plus COPEGUS.<sup>3,4</sup>

A sustained virological response means that the patient is virus-free six months after the end of therapy, and is considered cured of their hepatitis C.

### **HIV-HCV Co-infection**

- About 30% of people infected with HIV are also infected with HCV.<sup>5</sup>
- PEGASYS was the first, and is still the only approved treatment for hepatitis C in patients with HIV co-infection.<sup>6</sup>
  - This license was granted based on the results of the landmark study called APRICOT, the only multinational trial in this patient population to study the efficacy and safety of pegylated interferon combination therapy.
- In this difficult-to-treat population, 40% of patients who received PEGASYS plus COPEGUS (at a dose of 800 mg only) for 48 weeks were cured of their hepatitis C.<sup>7</sup>

### **Chronic Hepatitis C with Persistently Normal ALT Levels**

People with hepatitis C and persistently normal levels of alanine aminotransferase (ALT, a marker for liver inflammation) traditionally were not considered for treatment, as they were thought to have 'mild' disease only. Now we know that these people can, in fact, have severe liver damage as a consequence of their hepatitis C.<sup>8,9</sup>

- In the only multinational trial of its kind, 52% of patients treated with PEGASYS plus COPEGUS (800 mg only) achieved a cure.<sup>10</sup>

As a result, PEGASYS is the only pegylated interferon licensed in the EU for the treatment of these patients.<sup>6</sup>

### **Patients with Cirrhosis**

Liver damage can occur in patients with chronic hepatitis C, and can get progressively worse with time. PEGASYS is the only pegylated interferon tested in a trial specifically aimed at this difficult-to-treat population.<sup>11</sup>

### **Patients with Chronic Hepatitis B**

PEGASYS is also the only pegylated interferon licensed for the treatment of chronic hepatitis B.

Importantly, study results show no resistance in patients treated with PEGASYS alone, however in the same study 27% of patients treated with lamivudine developed resistance.<sup>12</sup>

### **Ease of Use and Tolerability**

Since interferon is a protein, it must be injected into the body, as the stomach would break it down if it were taken orally.

PEGASYS is the only ready-to-use pre-filled syringe for hepatitis C treatment. It is administered once-a-week, and both patients and doctors agree that it is more user friendly than an injector pen.<sup>13</sup>

PEGASYS is delivered as a fixed dose for all patients, thus there is no need to adjust the dose according to body weight.

The properties of PEGASYS lead to less frequent side effects such as flu-like symptoms, fatigue and depression, compared with conventional interferon treatment.<sup>14</sup> With fewer side effects, patients are more likely to stay on therapy, increasing their chance of a cure.

#### References

1. Hadziyannis SJ, Sette H, Jr., Morgan TR, et al. Peginterferon-alpha2a and ribavirin combination therapy in chronic hepatitis C: a randomized study of treatment duration and ribavirin dose. *Ann Intern Med* 2004;140(5):346-55.
2. National Institutes of Health Consensus Development Conference Statement: Management of hepatitis C: 2002--June 10-12. *Hepatology* 2002;36(5 Suppl 1):S3-20.
3. Diago M, Hassanein T, Rodes J, Ackrill AM, Sedarati F. Optimized virologic response in hepatitis C virus genotype 4 with peginterferon-alpha2a and ribavirin. *Ann Intern Med* 2004;140(1):72-3.
4. Thakeb F, Omar M, El Awady M, Isshak S. Randomized controlled trial of peginterferon alfa-2a plus ribavirin for chronic hepatitis C virus genotype 4 among Egyptian patients. *Hepatology* 2003;38(4 (Suppl 1)):278A-9A.
5. Alberti A, Clumeck N, Collins S, et al. Short statement of the first European Consensus Conference on the treatment of chronic hepatitis B and C in HIV co-infected patients. *J Hepatol* 2005;42(5):615-24.
6. PEGASYS® EMEA Summary of Product Characteristics. <http://www.eudra.org/humandocs/Humans/EPAR/PEGASYS/PEGASYS.htm>. 2004.
7. Torriani FJ, Rodriguez-Torres M, Rockstroh JK, et al. Peginterferon Alfa-2a plus ribavirin for chronic hepatitis C virus infection in HIV-infected patients. *N Engl J Med* 2004;351(5):438-50.
8. Bacon BR. Treatment of patients with hepatitis C and normal serum aminotransferase levels. *Hepatology* 2002;36(5 Suppl 1):S179-84.
9. Puoti C, Castellacci R, Montagnese F. Hepatitis C virus carriers with persistently normal aminotransferase levels: healthy people or true patients? *Dig Liver Dis* 2000;32(7):634-43.
10. Zeuzem S, Diago M, Gane E, et al. Peginterferon alfa-2a (40 kilodaltons) and ribavirin in patients with chronic hepatitis C and normal aminotransferase levels. *Gastroenterology* 2004;127(6):1724-32.
11. Heathcote EJ, Shiffman ML, Cooksley WG, et al. Peginterferon alfa-2a in patients with chronic hepatitis C and cirrhosis. *N Engl J Med* 2000;343(23):1673-80.
12. Lau GK, Piratvisuth T, Luo KX, et al. Peginterferon alfa-2a (40KD) (PEGASYS®) monotherapy and in combination with lamivudine is more effective than lamivudine monotherapy in HBeAg-positive chronic hepatitis B: Results from a large, multinational study. In: 55th Annual Meeting of the American Association for the Study of Liver Diseases; 2004; Boston, MA; 2004.
13. Janisch H. Economic evaluation of standard-therapy for chronic hepatitis C with Peginterferon alfa-2 (40KD)(PegIFN 2a) plus Ribavirin versus Peginterferon alfa-2b (12KD) (PegIFN 2b) plus Ribavirin: Ready-to-use syringe (SYR) versus injector (INJ) (SPRINT) *Hepatology* 2005;42 (Suppl. 1):648A.
14. Fried MW, Shiffman ML, Reddy KR, et al. Peginterferon alfa-2a plus ribavirin for chronic hepatitis C virus infection. *N Engl J Med* 2002;347(13):975-82.