HAUTE AUTORITÉ DE SANTÉ

The legally binding text is the original French version

TRANSPARENCY COMMITTEE

OPINION

15 March 2006

Pegasys 135 mcg, solution for injection in prefilled syringe
Box of 1 (CIP code: 359 958-1)

Pegasys 135 mcg, solution for injection in prefilled syringe
Box of 4 (CIP code: 359 959-8)

Pegasys 180 mcg, solution for injection in prefilled syringe
Box of 1 (CIP code: 359 960-6)

Pegasys 180 mcg, solution for injection in prefilled syringe
Box of 4 (CIP code: 359 961-2)

Applicant: Roche Laboratories

peginterferon alpha-2a

List I
Medicinal product requiring close monitoring during treatment.
Medicinal product subject to six-monthly prescription initially, reserved for specialists and/or departments specialising in gastroenterology, hepatology, internal medicine or infectious disease.
Unrestricted renewal.

Medicine dispensed in both pharmacies and hospitals.
Listed as a medicine which can be sold by hospitals to outpatients.

Date of Marketing Authorisation and amendments to Marketing Authorisation: 20 June 2002, 23 July 2003, 29 October 2004, 26 January 2005, 23 February 2005.

Reason for request:

- **Extension of indication in the treatment of HBeAg positive or negative chronic hepatitis B in adults with compensated liver disease.**

- **Extension of indication in the treatment of chronic hepatitis C in adults coinfected with HIV (stable HIV infection), who are serum HCV-RNA positive, including patients with compensated cirrhosis.**

1 CHARACTERISTICS OF THE MEDICINAL PRODUCT

1.1. Active ingredient

peginterferon alpha-2a

1.2. Background

This is the first pegylated interferon indicated in the treatment of chronic hepatitis B.

1.3. Indications

Chronic hepatitis B (**Extension of indication**)
Pegasys is indicated in the treatment of HBeAg positive or negative chronic hepatitis B in adults with compensated liver disease with viral replication, increased ALT and histologically confirmed liver inflammation and/or fibrosis.

Chronic hepatitis C
Pegasys is indicated in the treatment of chronic hepatitis C in adults who are serum HCV-RNA positive, including patients with compensated cirrhosis **and/or patients coinfected with HIV (stable HIV infection). (Extension of indication)**

The best way to use Pegasys in patients with chronic hepatitis C is in combination with ribavirin. This combination is indicated both in naive patients and in patients who have previously responded to alpha interferon and then relapsed after the end of treatment .

Monotherapy is mainly indicated in patients intolerant of or with contraindications to ribavirin.

1.4. Recommended dosage and duration of therapy

The therapy should be initiated only by a doctor with experience in treating patients with hepatitis B or C. When Pegasys is used in combination with ribavirin, consult the SPC for ribavirin.

Chronic hepatitis B: 180 mcg once weekly for 48 weeks, by subcutaneous injection in the abdomen or thigh, for both HBeAg positive and HBeAg negative chronic hepatitis B.

Chronic hepatitis C: 180 mcg once weekly, by subcutaneous injection in the abdomen or thigh, in combination with ribavirin or in monotherapy.

The dose of ribavirin to be used in combination with Pegasys is given in Table 1. Ribavirin should be taken with food.

The duration of therapy for chronic hepatitis C in combination with ribavirin depends on the viral genotype. Patients infected with HCV genotype 1 should be treated for 48 weeks whatever the viral load. Patients infected with HCV genotype 2/3 should be treated for 24 weeks whatever the viral load (see Table 1).

Table 1. Recommended combined dosages in HCV-infected patients

Genotype	Pegasys dose	Ribavirin dose	Duration
Genotype 1	180 mcg	< 75 kg = 1000 mg ≥ 75 kg = 1200 mg	48 weeks 48 weeks
Genotype 2/3	180 mcg	800 mg	24 weeks

In general, patients infected with genotype 4 are considered difficult to treat, and the limited trial data (n = 66) are compatible with a dosage identical to that used for genotype 1. The presence of others risk factors should also be taken into account when deciding the duration of therapy. This dosage should also be considered for patients infected with genotypes 5 or 6.

In monotherapy, the recommended duration of therapy with Pegasys is 48 weeks.

Coinfection with HIV and HCV

The recommended dosage of Pegasys, alone or in combination with 800 mg of ribavirin, is 180 mcg once weekly for 48 weeks, by the subcutaneous route, whatever the genotype. The safety and efficacy of combining Pegasys with ribavirin doses over 800 mg/day, or therapy lasting less than 48 weeks, have not been investigated.

Predictive value of obtaining a response or lack of response.

Obtaining an early virological response at week 12, defined as a 2 log decrease in viral load or no detected HCV RNA, is predictive of a sustained response.

Table 2. Predictive value of virological response at the recommended dosage in combined therapy with Pegasys

	Negative			**Positive**		
	Absence of response at week 12	Absence of sustained response	Predictive value	Response at week 12	Sustained response	Predictive value
Genotype 1 (n = 569)	102	97 (97/102)	**95%**	467	271 (271/467)	**58%**
Genotype 2/3 (n = 96)	3	3 (3/3)	**100%**	93	81 (81/93)	**87%**

In patients treated with Pegasys monotherapy, the predictive value of an absence of sustained response was 98%.

A similar negative predictive value was seen in HIV-HCV coinfected patients taking Pegasys alone or in combination with ribavirin (100% (130/130) and 98% (83/85) respectively). In coinfected patients treated with combined therapy, positive predictive values of 45% (50/110) and 70% (59/84) respectively were seen for genotypes 1 and 2/3.

For modification of the dose in patients with undesirable reactions, and special populations, see SPC.

2 SIMILAR MEDICINAL PRODUCTS

2.1. ATC Classification (2005)

L : ANTINEOPLASTIC AND IMMUNOMODULATING AGENTS
L03 : IMMUNOSTIMULATING AGENTS
L03A : CYTOKINES AND IMMUNOMODULATING AGENTS
L03AB : INTERFERONS
L03AB11 : peginterferon alpha-2a

2.2. Medicines in the same therapeutic category

2.2.1. Comparator drugs

Treatment of chronic hepatitis B
Pegasys is the only pegylated interferon indicated in the treatment of chronic hepatitis B.
Nonpegylated alpha interferons:

interferon α 2a: Roferon-A 3 MIU, 4.5 MIU, 6 MIU, 9 MIU, 18 MIU
interferon α 2b: Intron A

Treatment of chronic hepatitis C
Peginterferon alpha 2b: Viraferonpeg 50 mcg, 80 mcg, 100 mcg, 120 mcg, 150 mcg (powder and solvent for solution for injection in prefilled pen).
Nonpegylated alpha interferons:

interferon α 2a: Roferon-A 3 MIU, 4.5 MIU, 6 MIU, 9 MIU, 18 MIU
interferon α 2b: Intron A
interferon α 2b: Viraferon 3 MIU, 18 MIU
interferon alphacon-1: Infergen 9 mcg

2.3. Medicines in the same therapeutic area

Treatment of chronic hepatitis B
nucleoside and nucleotide analogues:

lamivudine – Zeffix
adefovir – Hepsera

3 ANALYSIS OF AVAILABLE DATA

A. Extension of indication in the treatment of HBeAg positive or negative chronic hepatitis B in adults with compensated liver disease

Two controlled trials (WV 16240[1], and WV 16241[2]) compared the safety and efficacy of Pegasys (180 mcg/week) with the combination Pegasys plus lamivudine (100 mg/day), and with lamivudine alone (100 mg/day) for 48 weeks in the treatment of HBe antigen positive or negative chronic hepatitis B.

Trial WV 16240 was conducted in 820 patients infected with a wild-type hepatitis B virus (HBeAg +), most of whom were Asian (85-87%).

Trial WV 16241 was conducted in 552 patients infected with a mutant virus (HBeAg -) of whom 61% were Asian and 37% Caucasian.

Both trials enrolled patients over 18 years old with compensated liver disease, active viral replication quantified by HBV DNA count, increased ALT levels and histological hepatic lesions compatible with chronic hepatitis. Patients coinfected with HBV and HIV were not included in these trials.

In t trial WV16240, the primary endpoints were HBeAg seroconversion (loss of HBeAg and development of anti-HBe antibodies) and existence of a sustained virological response (HBV DNA less than 10^5 copies/mL) 24 weeks after the end of treatment.(week 72).

[1] Lau GK *et al.* Peginterferon alfa-2a, lamivudine, and the combination for HBeAg-Positive Chronic Hepatitis B, *N Engl J Med* 2005;352:2682-2695
[2] Marcellin P. Peginterferon alfa-2a alone, lamivudine, and the two in combination in patients with HBeAg-negative chronic hepatitis B, *N Engl J Med* 2004;351:1206-1217

In trial WV16241 the primary endpoints were sustained biochemical response (ALT normalisation) and sustained virological response (HBV DNA less than 2 x 10^4 copies/mL) 24 weeks after the end of treatment (week 72).

Around 85–95% of patients completed the follow-up period (week 72).

Efficacy

Serological, virological, biochemical and histological responses 24 weeks after the end of treatment (week 72)

	Trial WV16240: HBeAg positive % response			**Trial WV16241: HBeAg negative % response**		
	Pegasys 180 mcg & **placebo**	**Pegasys** 180 mcg & **Lamivudine** 100 mg	**Lamivudine** 100 mg	**Pegasys** 180 mcg & **placebo**	**Pegasys** 180 mcg & **Lamivudine** 100 mg	**Lamivudine** 100 mg
n	271	271	272	177	179	(181
Primary endpoints						
HBeAg seroconversion	32#	27	19	N/A	N/A	N/A
Virological response*	32#	34	22	43#	44	29
ALT normalisation	41#	39	28	59#	60	44
Secondary endpoints						
HBsAg seroconversion	3#	3	0	3#	2	0
Histological response**	49	52	51	59	48	58

* for HBeAg+ patients: HBV DNA < 10^5 copies/mL; for HBeAg- patients: HBV DNA < 2 x 10^4 copies/mL
HBV DNA measured by the COBAS AMPLICOR™ HBV MONITOR test (detection limit 200 copies/mL)
** percentage of patients with an improved HAI score ≥ 2 points (Ishak), without worsening of fibrosis
# value of p (compared to lamivudine) < 0.01 (Cochran-Mantel-Haenszel test)
N/A: Not available

Safety

Adverse events occurred in 88% of patients treated with Pegasys alone or in combination with lamivudine, compared with 53% of patients treated with lamivudine alone.

The most common effects in patients given Pegasys were those known to occur with pegylated interferon in chronic hepatitis C: fever, fatigue, headache, myalgia, alopecia, dizziness, nausea, pruritis, athralgia, diarrhoea, insomnia, rash, tremor, asthenia, anorexia and loss of appetite. There were fewer adverse events in patients with chronic hepatitis B. Depression was less common than in patients with HCV (5% compared with 20–25%).

Serious adverse events occurred in 6% of patients treated with Pegasys and 4% of patients treated with lamivudine. In the Pegasys group, 5% of patients discontinued therapy because of adverse events or laboratory test abnormalities, whereas less than 1% of patients in the group given lamivudine alone discontinued therapy because of adverse events.. Discontinuation rates in patients with cirrhosis were similar to those for the overall population in each treatment group.

Experience acquired in clinical trials (see SPC)

The frequency and severity of the main undesirable reactions with Pegasys were similar to those reported with nonpeglyated interferon alpha-2a. The most common adverse events with Pegasys 180 mcg were mainly mild to moderate and did not require changes in dose or discontinuation of therapy.

Conclusion

The efficacy and safety of Pegasys in treating chronic hepatitis B were assessed in adult patients with compensated liver disease, active viral replication, increased ALT levels and histological hepatic lesions compatible with chronic hepatitis.

After 48 weeks of treatment and 24 weeks of treatment free follow-up (week 72), virological, biochemical and serological responses were significantly more common in patients taking Pegasys than in patients taking lamivudine (absolute difference of around 10 points).

In patients infected with a wild-type virus (HBeAg positive), HBe seroconversion (loss of HBeAg and development of anti-HBe antibodies) was seen in 32% of patients treated with Pegasys and 19% of patients treated with lamivudine ($p < 0.001$). A sustained virological response (HBV DNA less than 10^5 copies/mL) was seen in 32% of patients treated with Pegasys and 22% of patients treated with lamivudine ($p = 0.012$).

In patients infected with a mutant virus (HBeAg negative), a sustained virological response (HBV DNA less than 2×10^4 copies/mL) was seen in 43% of patients treated with Pegasys and 29% of patients treated with lamivudine ($p = 0.007$).

A sustained biochemical response (ALT normalisation) was seen in 59% of patients treated with Pegasys and 44% of patients treated with lamivudine ($p = 0.004$).

In both trials, HBs seroconversion was seen only in patients treated with Pegasys (3%). The histological response was similar to that achieved with lamivudine therapy.

The combination of lamivudine with Pegasys conferred no therapeutic benefit over Pegasys monotherapy.

The safety profile of Pegasys is comparable to that seen in the treatment of hepatitis C. It is similar to that of nonpegylated alpha interferons. Severe adverse events especially psychiatric effects, are no more frequent. Safety is inferior to that of lamivudine.

B. Extension of indication: treatment of adult patients coinfected with HIV (stable HIV infection), with serum positive HCV RNA, including patients with compensated cirrhosis

The efficacy and safety of Pegasys alone or in combination with ribavirin were assessed in an open-label trial in 868 HIV-HCV coinfected patients (trial NR 15961). Patients were randomised into three treatment arms:

- Pegasys 180 mcg/week + placebo
- Pegasys 180 mcg/week + ribavirin 800 mg/day
- Roferon-A 3 MIU 3 times/week + ribavirin 800 mg/day

Treatment lasted 48 weeks with a 24-week follow-up period without treatment.

Primary endpoint: sustained virological response, defined as no detectable HCV RNA (< 50 IU/mL) 24 weeks after the end of treatment (depending on viral genotype). HCV RNA was measured using the COBAS AMPLICOR™ HCV test, version 2.0 (detection limit 100 copies/mL, i.e. equivalent to 50 International Units/mL).

Characteristics of patients enrolled

The trial covered patients over 18, who had never been treated with interferon and who had:

- chronic hepatitis C confirmed by detectable serum HCV RNA levels, increased ALT and liver biopsy compatible with chronic hepatitis. Around 15% of patients had cirrhosis (METAVIR score F3 or F4). Genotype distribution was similar to that seen in patients with HCV monoinfection (60% infected with genotype 1 and 40% with a non-1 genotype),
- and stable HIV infection with a mean CD4 count of 500/mcL (more than 90% of patients had a CD4 count > 200/mm^3). Sixty percent of patients had an undetectable viral load

(< 50 copies/mL). The majority of patients (85%) were taking highly active antiretroviral multitherapy.

Efficacy

Sustained virological response according to genotype and viral load in HIV-HCV coinfected patients

	Responders - % (ratio)		
	Pegasys 180 mcg + ribavirin 800 mg n = 289	Pegasys 180 mcg n = 286	Roferon-A 3 MIU + ribavirin 800 mg n = 285
All patients	40 (116/289)*	20 (58/286)*	12 (33/285)*
Genotype 1	29 (51/176)	14 (24/175)	7 (12/171)
Low viral load	61 (28/46)	38 (17/45)	19 (8/42)
High viral load	18 (23/130)	5 (7/130)	3 (4/129)
Genotype 2-3	62 (59/95)	36 (32/90)	20 (18/89)
Low viral load	61 (17/28)	38 (9/24)	27 (8/30)
High viral load	63 (42/67)	35 (23/66)	17 (10/59)
Genotype 4	(6/16)	(1/20)	(3/24)

* Pegasys 180 mcg + ribavirin 800 mg versus interferon alfa-2a 3 MIU + ribavirin 800 mg: OR (CI 95%) = 5.40 (3.42 - 8.54), p < 0.0001 (Cochran-Mantel-Haenszel test)
* Pegasys 180 mcg + ribavirin 800 mg versus Pegasys 180 mcg: OR (CI 95%) = 2.89 (1.93 – 4.32), p < 0.0001
* Roferon-A 3 MIU + ribavirin 800 mg versus Pegasys 180 mcg: OR (CI 95%) = 0.53 (0.33 – 0.85), p = 0.0084

Thirty percent (13/44) of patients with cirrhosis (F3 or F4) achieved a sustained virological response with Pegasys/ribavirin therapy.

Undesirable effects

Safety profile in HIV-HCV coinfected patients (% patients)

	Pegasys 180 mcg		
	& **Ribavirin 800 mg** 48 weeks **HIV-HCV Coinfection**	& **Ribavirin 800 mg** 24 weeks **HCV monoinfection**	& **Ribavirin 1000/1200 mg** 48 weeks **HCV monoinfection**
Serious adverse events	17	3	11
Anaemia (Haemoglobin < 10 g/dL)	14	3	15
Ribavirin dose modification	37	19	39
Withdrawal from trial due to adverse events	12	4	10
Withdrawal from trial due to abnormal laboratory results	3	1	3

Pegasys therapy was associated with a decrease in absolute CD4 count in the first 4 weeks of treatment. This decrease in CD4 count was reversible after a decrease in dosage or discontinuation of therapy. No negative impact on HIV viral load control was seen during Pegasys therapy or the follow-up period.

Limited safety data (n = 31) were available in co-infected patients with CD4+ cell counts < 200/mcl.

Severe neutropenia (< 500 neutrophils/mm^3) was more frequent in the groups including Pegasys: 13% of patients on Pegasys/ribavirin, 11% on Pegasys alone, and fewer than 1% in the Roferon-A/ribavirin arm. The same was true of anaemia (haemoglobin < 10 g/dL): 14% on Pegasys/ribavirin, 8% on Pegasys alone, and 4% on Roferon-A/ribavirin. Although these haematological disorders were more common in HIV-HCV coinfected patients, most could be

managed by modifying dose and/or using growth factors. These disorders only rarely required premature discontinuation of treatment.

Percentage onset of depression was comparable in all 3 treatment groups (20–26%). Most cases of depression were mild to moderate.

Clinical experience (see SPC)

In HIV-HCV coinfected patients, the clinical adverse event profile reported for Pegasys, alone or in combination with ribavirin, was similar to that observed in HCV monoinfected patients.

Conclusion

The efficacy and safety of Pegasys/ribavirin bitherapy in treating HIV-HCV coinfected patients were assessed in adult patients with chronic hepatitis C confirmed by detectable serum HCV RNA levels, increased ALT and liver biopsy compatible with chronic hepatitis and stable HIV infection.

After 48 weeks of treatment and 24 weeks of treatment-free follow-up (week 72), virological efficacy (sustained virological response) of Pegasys/ribavirin bitherapy was significantly superior to that of Pegasys alone (40% vs. 20%, $p < 0.0001$) and that of Roferon-A/ribavirin (40% vs. 12%, $p < 0.0001$), whatever the viral genotype.

Sustained virological response was higher in patients infected with genotype 2/3 (62%) than in those infected with genotype 1 (29%). However, patients with genotype 1 and a low viral load ≤ 800 000 IU/mL treated with Pegasys/ribavirin had a rate of sustained virological response similar to that in patients with genotype 2/3.

The safety profile was similar to that recorded in patients with HCV monoinfection. Pegasys/ribavirin bitherapy had no negative impact on the progression of HIV infection in terms of HIV viral load.

Limited safety data (n = 31) were available in coinfected patients with CD4+ cell counts < 200/mcl.

Efficacy and safety for the combination therapy with ribavirin doses over 800 mg/day or for less than 48 weeks' of treatment have not been studied.

The trial results confirm the superiority of Pegasys and ribavirin over dual therapy with standard interferon in the treatment of chronic hepatitis C.

4 TRANSPARENCY COMMITTEE CONCLUSIONS

4.1. Actual benefit

- Treatment of HBeAg positive or negative chronic hepatitis B in adults with compensated liver disease

Hepatitis B is a common viral disease which in its chronic form can progress to cirrhosis or hepatocellular carcinoma. Hepatitis B can be life-threatening. In fact, 15–25% of patients infected with HBV die from these serious complications.

The efficacy/safety ratio for Pegasys is moderate in this indication.

Pegasys monotherapy is used as curative first-line therapy.

There are alternative drugs.

Expected public health benefit

Hepatitis B is a moderate burden on public health. The burden represented by the population with the present indication is low because the number of patients is limited compared to the total population of patients with hepatitis B.

Reducing morbidity and mortality associated to chronic hepatitis B is a public health requirement. However, the clinical data do not suggest that Pegasys will offer an additional response to this need compared to current management of the disease.

It is not possible to estimate the impact of Pegasys on reducing the risk of complications or mortality from hepatitis B on the basis of the published trials, especially compared to nonpegylated interferon. All things considered, it is not expected that Pegasys will have an additional impact on morbidity and mortality compared to available therapies..

In view of the other treatments available, it is not expected that Pegasys will benefit public health in this indication.

The actual benefit of Pegasys is substantial.

- Treatment of HIV coinfected adult patients (stable HIV infection), with serum positive HCV RNA, including patients with compensated cirrhosis

The seriousness of chronic hepatitis C lies in the fact that it often progresses to chronic disease that can involve long-term complications such as cirrhosis, hepatocellular failure and hepatocellular carcinoma. In HIV-HCV coinfected patients, liver damage is more serious and cirrhosis develops twice as fast.

The efficacy/safety ratio of Pegasys in this indication is moderate.

Pegasys is used as curative first-line therapy in combination with ribavirin. In cases of intolerance or contraindication to ribavirin, Pegasys is used as monotherapy.

There are alternative drugs.

- Expected public health benefit

Hepatitis C is a moderate burden on public health. The burden represented by HIV-HCV coinfection is low because of the limited patient numbers concerned by the indication.

Reducing hepatitis C-linked morbidity and mortality is a public health requirement. It is not possible to determine whether Pegasys will offer a response to this requirement on the basis of the data available.

Data from the clinical trial conducted in HIV-HCV coinfected patients only showed the impact of Pegasys on the level of sustained virological response. The impact of Pegasys on reducing the risk of complications or mortality due to hepatitis C in coinfected patients cannot be estimated on the basis of the results for this intermediate endpoint.

In the current state of knowledge, it is not therefore expected that Pegasys will benefit public health in this indication.

The actual benefit of Pegasys in HIV-HCV coinfected patients is substantial.

4.2. Improvement in actual benefit

- Patients with HBeAg positive or negative chronic hepatitis B, **with compensated liver disease**

The superiority of Pegasys over standard alpha interferons has not been satisfactorily proven. The Committee considered that Pegasys does not offer any improvement in actual benefit (IAB V) compared to standard alpha interferon.

- Patients with chronic hepatitis C
Changes in the SPC relating to the treatment of adult patients coinfected with HCV and HIV (stable HIV infection) do not justify changing the previous Opinion (Committee Opinion of 20 November 2002).

4.3. Therapeutic use

4.3.1. Treatment of HBeAg positive or negative chronic hepatitis B in adults with compensated liver disease

In HBeAg positive or negative patients with moderate to severe hepatitis without cirrhosis, and patients with cirrhosis but no sign of decompensation, current opinion among hepatologists[3] is that initial therapy should be alpha interferon, and that nucleoside analogues (lamivudine - Zeffix) and nucleotide analogues (adefovir dipivoxil - Hepsera) should be reserved for patients with contraindications or who have failed alpha interferon therapy.

In a recent NICE publication [4] (National Institute for Health and Clinical Excellence) Pegasys is recommended as first-line therapy instead of nonpegylated alpha interferon.

4.3.2. Treatment of adult patients coinfected with HCV and HIV

According to the European consensus conference on the treatment of chronic hepatitis B and C in HIV-HCV or HIV-HBV coinfected patients[5]:

- the therapeutic approach takes account of the relative severity of HIV and HCV-related liver disease, to determine the order of priority of anti-HCV and anti-HIV therapy. Hepatitis C is not therefore treated in all patients, but only when the expected benefit of therapy outweighs the risks involved;
- the main objective of anti-HCV therapy is to achieve a sustained virological response (SVR) defined as an undetectable serum HCV RNA level at 24 weeks after the end of treatment.
  - Treatment is based on the bitherapy: pegylated interferon + ribavirin .
  - The dose of ribavirin varies according to the genotype and viral load:
    - ♦ 800 mg/day in patients with genotype 2/3, and patients with genotype 1 with a viral load ≤ 800 000 IU/mL
    - ♦ 1000–1200 mg/day in patients with genotype 1 and high viral load.
  - The currently recommended duration of therapy is 48 weeks whatever the genotype.
  - If there is no virological response after 12 weeks of treatment (reduction in viral load < 2 $\log_{10}$ copies/mL), treatment should be discontinued.
  - If HCV RNA is still detectable after 24 weeks of therapy, treatment should be discontinued.

4.4. Target population

- Treatment of HBeAg positive or negative chronic hepatitis B in adults with compensated liver disease
According to an InVS/CnamTS [6] survey of National Insurance contributors (general scheme) in 2003-2004, the prevalence of chronic hepatitis B in France in people aged 18–80 was 0.68%, i.e. around 300 000 people.

[3] EASL Jury. EASL international consensus conference on hepatitis B. J Hepatol 2003;38:533-540
[4] NICE. Adefovir dipivoxil and peginterferon alfa-2a for the treatment of chronic hepatitis B. Issued: 21st February 2006.
[5] Alberti *et al*. Short statement of the first European consensus conference on the treatment of chronic hepatitis B and C in HIV coinfected patients. J Hepatol 2005;42:615-624.

The treatment of chronic hepatitis B concerns only patients in the active phase of disease (30% of patients, according to expert opinion), i.e. 90 000 patients.

Furthermore, around 5% of patients with chronic hepatitis B have a contraindication to interferon (expert opinion).

The target population for Pegasys in chronic hepatitis B is thought to be 85 500 patients at most.

In practice, the number of patients likely to be given this therapy would probably be halved because, according to the InVS/CnamTS 2003-2004 survey, 49% of patients are not aware that they have HBV surface antigen (HBsAg).

- Treatment of adult patients coinfected with HCV and HIV

The estimated prevalence of HIV infection was around 100 000 people at the end of 2003 (source ANRS AC 23), and around 25% of HIV-infected patients have HCV, i.e. 25 000 people[7].

Around 69% of people with HCV are active carriers (HCV-RNA positive) and anti-HCV therapy is prescribed in around 36% of cases[8].

The target population for Pegasys in HIV-HCV coinfected patients is therefore around 7500 people.

4.5. Transparency Committee recommendations

The Committee recommended inclusion on the list of medicines reimbursed by National Insurance and approved for use by hospitals and various public services for the indications and at the dosages given in the Marketing Authorisation.

4.5.1. **Packaging**: Suitable for conditions of prescription.

4.5.2. **Rate of reimbursement:** 65%.

[6] *Estimation des taux de prévalence des anticorps anti-VHC et des marqueurs du virus de l'hépatite B chez les assurés sociaux du régime général de France métropolitaine*, *2003-2004*

[7] Delfraissy J-F *et al*. *Prise en charge thérapeutique des personnes infectées par le VIH – recommandations du groupe d'experts.* 2004 Report. Médecine Sciences Flammarion.

[8] BHE. *Prévalence des co-infections par le virus des hépatites B et C dans la population VIH+, France*, June 2004.