



CIGNA PHARMACY COVERAGE POLICY

The following Coverage Policy applies to all plans administered by CIGNA Companies including plans administered by Great-West Healthcare, which is now a part of CIGNA.

**Subject Peginterferon Alfa-2b
(PEG Intron®)**

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Alferon N®
 Infergen®
 Intron A®
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INSTRUCTIONS FOR USE

Coverage Policies are intended to provide guidance in interpreting certain **standard** CIGNA HealthCare benefit plans as well as benefit plans formerly administered by Great-West Healthcare. Please note, the terms of a participant's particular benefit plan document [Group Service Agreement (GSA), Evidence of Coverage, Certificate of Coverage, Summary Plan Description (SPD) or similar plan document] may differ significantly from the standard benefit plans upon which these Coverage Policies are based. For example, a participant's benefit plan document may contain a specific exclusion related to a topic addressed in a Coverage Policy. In the event of a conflict, a participant's benefit plan document **always supercedes** the information in the Coverage Policies. In the absence of a controlling federal or state coverage mandate, benefits are ultimately determined by the terms of the applicable benefit plan document. Coverage determinations in each specific instance require consideration of 1) the terms of the applicable group benefit plan document in effect on the date of service; 2) any applicable laws/regulations; 3) any relevant collateral source materials including Coverage Policies and; 4) the specific facts of the particular situation. Coverage Policies relate exclusively to the administration of health benefit plans. Coverage Policies are not recommendations for treatment and should never be used as treatment guidelines. Proprietary information of CIGNA. Copyright ©2011 CIGNA

Coverage Policy

CIGNA covers peginterferon alfa-2b (PEG Intron®) as medically necessary as monotherapy (age 18 years and older) or in combination with ribavirin (age 3 years old and older) for the treatment of Hepatitis C (HCV) in an individual with compensated liver disease, as indicated in the following chart:

Diagnosis	Treatment Authorization
Genotype 1	<ul style="list-style-type: none"> • 16 weeks - Initial authorization • Subsequent authorization(s) contingent on clinical response of at least a 2 log (100 fold decrease in quantitative HCV RNA by week 16 as follows: <ul style="list-style-type: none"> ➢ If HCV RNA is undetectable (< 50 IU/ml) at week 16, an additional 32 weeks (total 48 weeks) will be authorized ➢ If HCV RNA is detectable (> 50 IU/ml) at week 16, an additional 8 weeks will be authorized and HCV RNA re-evaluated at 24 weeks. An additional 48 -weeks (total 72 weeks) will be authorized if there is no detectable virus at 24 weeks (<50IU/ml)
Genotype 2 or 3	Standard treatment authorization - 24 weeks <ul style="list-style-type: none"> ➢ Genotype 3 with steatosis and initial high viral loads (HCV RNA >600,000 IU/mL) - authorize for 48 weeks

Genotype 4, 5, or 6	48 weeks
Bridging fibrosis or cirrhosis	48 weeks regardless of HCV genotype and changes in HCV RNA levels at week 12
Coinfection with human immunodeficiency virus (HIV)	48 weeks

When coverage is available and medically necessary, the dosage, frequency, site of administration, and duration of therapy should be reasonable, clinically appropriate, and supported by evidence-based literature and adjusted based upon severity, alternative available treatments, and previous response to Peginterferon Alfa-2b (PEG Intron[®]) therapy.

CIGNA does not cover peginterferon alfa-2b (PEG Intron[®]) for failure to respond to previous treatment with a full course of peginterferon alfa because it is considered experimental, investigational or unproven.

Note: PEG Intron is a non-preferred brand on the Great-West Healthcare Drug List. Therefore, PEG Intron is covered after failure, contraindication, or intolerance to Pegasys under Great West Healthcare benefits.

FDA Approved Indications

Combination Therapy

Peginterferon alfa-2b in combination with ribavirin is indicated for Chronic Hepatitis C (CHC) in patients ≥3 years with compensated liver disease. Patients with the following characteristics are less likely to benefit from retreatment after failing a course of therapy: previous nonresponse, previous pegylated interferon treatment, significant bridging fibrosis or cirrhosis, and genotype 1 infection

Monotherapy

Peginterferon alfa-2b monotherapy is indicated for CHC in patients (≥18 years) with compensated liver disease previously untreated with interferon alpha.

FDA Recommended Dosing

PegIntron/ribavirin Combination

Adults

The recommended dose is 1.5 mcg/kg/week subcutaneously in combination with 800 to 1400 mg of ribavirin orally. The treatment duration for patients with genotype 1 is 48 weeks. Discontinuation of therapy should be considered in patients who do not achieve at least a 2 log₁₀ drop or loss of HCV-RNA at 12 weeks, or if HCV-RNA remains detectable after 24 weeks of therapy. Patients with genotype 2 and 3 should be treated for 24 weeks. The treatment duration for patients who previously failed therapy is 48 weeks, regardless of HCV genotype. Retreated patients who fail to achieve undetectable HCV-RNA at week 12 of therapy, or whose HCV-RNA remains detectable after 24 weeks of therapy, are highly unlikely to achieve SVR and discontinuation of therapy should be considered.

Pediatric Patients

Dosing for pediatric patients is determined by body surface area for peginterferon alfa-2b and by body weight for ribavirin. The recommended dose of peginterferon alfa-2b is 60mcg/m²/week subcutaneously in combination with ribavirin 15 mg/kg/day of orally in two divided doses for pediatric patients ages 3 to 17 years. Patients who reach their 18th birthday while receiving peginterferon alfa-2b / ribavirin, should remain on the pediatric dosing regimen. The treatment duration for patients with genotype 1 is 48 weeks. Patients with genotype 2 and 3 should be treated for 24 weeks.

PegIntron Monotherapy

The recommended dose of peginterferon alfa-2b regimen is 1 mcg/kg/week subcutaneously for 1 year administered on the same day of the week. Discontinuation of therapy should be considered in patients who do not achieve at least a 2 log₁₀ drop or loss of HCV-RNA at 12 weeks of therapy, or whose HCV-RNA levels remain detectable after 24 weeks of therapy. The volume of PegIntron to be injected depends on patient weight

Black Box Warnings

Alpha interferons, including PegIntron, may cause or aggravate fatal or life-threatening neuropsychiatric, autoimmune, ischemic, and infectious disorders. Patients should be monitored closely with periodic clinical and laboratory evaluations. Patients with persistently severe or worsening signs or symptoms of these conditions should be withdrawn from therapy. In many, but not all cases, these disorders resolve after stopping PegIntron therapy

Drug Availability

Peginterferon alfa-2b is available in single-use vial and Redipen, an injectable pen.

General Background

Pharmacology/Pharmacokinetics

Several types of interferon (IFN) are utilized in the treatment of Hepatitis C (HCV). These include interferon alfa-2b, interferon alfacon, interferon alfa N, and two forms of pegylated interferon alfa. There is no convincing data to indicate a significant clinical difference between the various alpha interferons. Interferon alfa-2b is similar to interferon alfa-2a in that both are pure clones of single interferon subspecies. In pegylated interferons, polyethylene glycol (PEG) is attached to interferon as a protein modifying agent to decrease renal clearance and extend duration of action. This allows for once-weekly administration. Peginterferon alfa-2b has an approximately seven-fold lower mean apparent clearance and a five-fold greater mean half-life than interferon alfa-2b, allowing a reduced dosing frequency.

Peginterferon alfa drugs (PEG-IFN alfa-2a and PEG-IFN alfa-2b) are the only currently U.S. Food and Drug Administration (FDA)-approved pegylated interferon products on the market. The FDA approved these agents for the treatment of adult patients who have both chronic hepatitis C and are classified as having compensated liver disease who are interferon-naïve or who have relapsed or failed to respond to prior therapy with non-pegylated interferon. Compensated liver disease is defined as the presence of liver disease with either few symptoms or symptoms that are classified as mild and stable.

Guidelines

The American Gastroenterological Association and American Association for the Study of Liver Disease (AASLD) Practice Guidelines recommend antiviral therapy in patients with compensated liver disease and laboratory parameters including: total bilirubin level < 1.5 mg/100 mL; prothrombin time < 15 seconds [international normalized ratio, ≤ 1.7]; albumin level > 3.4 g/100 mL; with no history of ascites, bleeding esophagogastric varices, or hepatic encephalopathy. Patients presenting with ascites, bleeding varices or hepatic encephalopathy (decompensated liver disease) should be referred for consideration of liver transplantation. Additionally, per the manufacturer label approved by the FDA, the use of peginterferon alfa is contraindicated in patients with chronic hepatitis C virus (HCV) infection, with or without human immunodeficiency virus (HIV) coinfection, who demonstrate hepatic decompensation (Child-Pugh score > 6; class B and C) prior to or during treatment.

The following recommendations are based on practice guidelines (Strader, et al., 2004) supported by the AASLD, the Infectious Diseases Society of America, the American College of Gastroenterology, and the American Gastroenterological Association Technical Review on the Management of Hepatitis C (2006). However, these recommendations are designed to be flexible rather than rigidly inflexible and are intended to guide physicians and other health care workers to make logical patient care decisions. These recommendations should be followed in most cases; however, management decisions for individual patients are left to physicians and health care workers.

The goal of HCV treatment is to eradicate the virus and prevent progression to end-stage liver disease. Prior to treatment, HCV genotype should be determined in all persons by serologic immunoassay or molecular determination. The HCV genotype will determine the duration of therapy and likelihood of response. There are currently six known HCV genotypes. The majority of patients within the United States have genotype 1 (70%–80%), with the remainder presenting with genotypes 2 and 3 (20%–30%). Patients with genotype 4, 5 and 6 are uncommonly encountered in the United States. Currently, combination therapy with oral ribavirin and pegylated-interferon is the standard of care for the treatment of chronic hepatitis C. Combination therapy of pegylated-

interferon and ribavirin has demonstrated superior effectiveness compared to interferon alfa alone in interferon-naïve patients.

A valuable clinical milestone for monitoring the response to antiviral therapy in patients with genotype 1 is an early virologic response (EVR), which is defined as ≥ 2 log (100-fold) decrease in quantitative HCV ribonucleic acid (RNA) levels during the first 12 weeks of therapy. Therefore, baseline and 12-week monitoring of HCV RNA levels should be performed on all patients diagnosed with HCV genotype 1.

Genotype 1 patients are generally more treatment-refractory [sustained virologic response (SVR) ≤ 40 -50%]; therefore, a full 48 weeks of therapy in combination with maximum doses of ribavirin (1000–1200 mg/day) is recommended. Quantitative serum HCV RNA should be performed at the initiation of, or shortly before, treatment and at week 12 of therapy. If patients do not achieve an EVR at 12 weeks, the treatment may be discontinued, since 97% of patients who do not achieve an EVR will fail to develop an SVR. However, in order to obtain the lab value, CIGNA HealthCare allows an approval of 16 weeks initial authorization. An additional 32 weeks (total 48 weeks) will be authorized if there is at least a 2 log (100- fold) decrease in quantitative HCV ribonucleic acid (RNA) which is usually drawn on week 12 but no later than week 16. There will be no additional authorization past the initial 16 weeks if there is less than a 2 log decrease in HCV RNA. Patients whose treatment continues through 48 weeks and whose qualitative measurement of HCV RNA at that time is negative should be retested for HCV RNA 24 weeks later to document an SVR. An additional 56 weeks (total 72 weeks) will be authorized if patient is identified as slow virologic responder who has an EVR with a 2 log drop but detectable virus (>50 IU/ml) at 12 weeks and has no detectable virus at 24 weeks (<50 IU/ml).

For genotype 2 and 3 patients who demonstrate a more treatment-favorable response to therapy (SVR $\geq 80\%$), 24 weeks of therapy with peginterferon plus ribavirin should be administered, using a ribavirin dose of 800 mg per day. Patients whose treatment continues for the full 24 weeks, and whose qualitative measurement of HCV RNA at that time is negative, should be retested for HCV RNA 24 weeks later to document an SVR.

Studies have shown that there is a direct viral mechanism involved in the development of steatosis in people infected with HCV genotype 3. Steatosis, known as fatty liver, is a condition characterized by the accumulation of fat in the liver. Steatosis appears to increase the rate of HCV disease progression. Recent studies have shown that higher grades of steatosis correlate with higher grades of fibrosis, and with more rapid development of fibrosis and cirrhosis. On the basis of available evidence, genotype 3 patients with Steatosis and high viral loads (HCV RNA $>600,000$ IU/mL) may need longer duration of treatment, and therapy should be continued for the full 48 weeks.

There is insufficient experience to provide recommendations for treatment of persons with genotypes 4, 5, and 6. In the absence of any clinical trial including a sufficient number of patients, the likelihood of an SVR and the optimal treatment schedule remain unknown for patients infected with HCV genotypes 4, 5 or 6. It is thus recommended to treat them like those infected with HCV genotype 1 (i.e., pegylated IFN alfa, in combination with high-dose ribavirin (1000–1200 mg per day). In the absence of published data, no stopping rules have been defined, and it is recommended these patients be treated for a total of 48 weeks.

Patients with compensated cirrhosis or advanced fibrosis who can tolerate and respond to therapy should be considered candidates for therapy. Response rates observed in patients with bridging fibrosis and cirrhosis have increased (approximately 40%) with the introduction of IFN/ribavirin combination regimens. PEG-IFN plus ribavirin is recommended in this subpopulation, as it is in noncirrhotic patients.

The National Institute of Health (NIH) consensus statement on HCV states that pegylated-interferons in combination with ribavirin is an appropriate therapy for nonresponders (defined as patients who fail to respond to a previous course of standard IFN, with or without ribavirin) and relapsers (defined as patients in whom HCV RNA is undetectable during and at the end of therapy but reappears again after completion of therapy). Generally, an SVR can be achieved by re-treatment with peginterferon alfa and ribavirin in 25–40% of persons who failed to respond to interferon alfa monotherapy and in about 10% who failed to respond to interferon alfa and ribavirin. The chance of achieving an SVR in relapsers may be as high as 40–50% if re-treatment is pursued with more effective therapy. Therapy with peginterferon and ribavirin should be strongly considered for patients who experienced a relapse after a course of standard IFN/ribavirin combination therapy.

Patients who are coinfecting with Hepatitis C and HIV should be considered as candidates for therapy. Regardless of genotype, the optimal therapy consists of PEG-IFN alfa at the routine weekly dose plus ribavirin at a daily dose of 600–800 mg for 48 weeks. Due to potential drug-drug interactions, if didanosine is critical to the HIV regimen, ribavirin should be avoided.

To date, no recommendation can be made regarding maintenance therapy. Several randomized, controlled, phase III studies with low-dose PEG-IFN are in progress to evaluate the effect of maintenance therapy on histologic and clinical end points in patients with chronic hepatitis C.

To date, there is no recommendation regarding the extension of treatment duration beyond 48 weeks. However, two open-labeled studies evaluated the potential benefits of extending treatment from 48 to 72 weeks with peginterferon- α 2a plus ribavirin. One study found that patients with detectable HCV RNA after four weeks of therapy could benefit from extending therapy from 48 to 72 weeks. The second study found that in patients classified as 'slow viral response' (positive HCV RNA at week 12 with between 50 to 5,000 IU/mL, but negative HCV RNA at week 24), extension of therapy beyond 48 weeks could reduce relapse rates and improve sustained response rates.

Clinical Studies

In open-label and comparative trials, patients treated with peginterferon alfa-2b demonstrated a greater sustained viral response in a dose-related manner compared to non-pegylated interferon alfa-2b. A total of 1219 adults with chronic hepatitis from HCV infection were evaluated in a randomized study comparing treatment with peginterferon alfa-2b to treatment with interferon alfa-2b, recombinant. Patients were treated for 48 weeks and were followed for 24 weeks post-treatment. Seventy percent of all patients were infected with HCV genotype 1, and 74% of all patients had high baseline levels of HCV RNA (more than two million copies/ml of serum), two factors known to predict poor response to treatment. Patients with both viral genotype 1 and high serum levels of HCV RNA at baseline were less likely to respond to treatment with peginterferon alfa-2b. Among patients with the two unfavorable prognostic variables, 8% (12/157) responded to peginterferon alfa-2b treatment, and 2% (4/169) responded to interferon alfa-2b, recombinant. Doses of peginterferon alfa-2b higher than the recommended dose did not result in higher response rates in these patients. Patients receiving peginterferon alfa-2b with viral genotype 1 had a response rate of 14% (28/199), while patients with other viral genotypes had a 45% (43/96) response rate. Ninety-six percent (96%) of the responders in the peginterferon alfa-2b groups and 100% of responders in the interferon alfa-2b recombinant group first cleared their viral RNA by week 24 of treatment.

Combination therapy with peginterferon alfa-2b and ribavirin in 1530 adults with chronic hepatitis C showed superior results over peginterferon alfa-2b alone. A randomized study compared treatment with two peginterferon alfa-2b/ribavirin regimens [peginterferon alfa-2b 1.5 ug/kg subcutaneous (SC) once weekly (qw)/ribavirin 800 mg daily (in divided doses); peginterferon alfa-2b 1.5 ug/kg SC qw for four weeks, then 0.5 ug/kg SC qw for 44 weeks/ribavirin 1000/1200 mg daily (in divided doses)] with interferon alfa-2b, recombinant [3 milli - international units (MIU) SC three times weekly (tiw)/ribavirin 1000/1200 mg daily (in divided doses)]. Interferon-naïve patients were treated for 48 weeks and followed for 24 weeks post-treatment. The response rate to the peginterferon alfa-2b 1.5 ug/kg plus ribavirin 800 mg dose was higher than the response rate to interferon alfa-2b, recombinant/ribavirin. The response rate to peginterferon alfa-2b 1.5-0.5 ug/kg/ribavirin was essentially the same as the response to interferon alfa-2b, recombinant/ribavirin. Patients with viral genotype 1, regardless of viral load, had a lower response rate to peginterferon alfa-2b (1.5 ug/kg)/ribavirin compared to patients with other viral genotypes. Patients with both poor prognostic factors (genotype 1 and high viral load) had a response rate of 30% (78/256) compared to a response rate of 29% (71/247) with interferon alfa-2b, recombinant/ribavirin.

In a randomized controlled study, Hadziyannis et al. (2004) evaluated both the duration of treatment and the dose of ribavirin. Patients were randomized into four groups to be treated for either 24 or 48 weeks and to receive either 800 mg daily or 1000–1200 mg daily (based on weight) of ribavirin plus PEG-IFN alfa-2a (180 mcg once a week). In this study, a high frequency of SVR occurred in patients with genotypes 2 and 3, regardless of the regimen, but optimal frequencies of SVR in genotype 1 (52%) required longer-duration and full-dose ribavirin, independent of the level of HCV RNA. In this study, the levels of HCV RNA had little impact on frequency of SVR in patients with genotypes 2 and 3. SVR in patients with genotype 1 treated for a full 48 weeks and with full-dose ribavirin was only 47% for those with HCV RNA levels greater than 2 million copies/mL but as high as 65% for those with HCV RNA levels \leq 2 million copies/mL. Results showed that patients with

genotype 1 require 48 weeks of therapy with higher doses of ribavirin in combination with peginterferon, while patients with genotypes 2 and 3 can be treated for only 24 weeks and with only 800 mg daily of ribavirin.

Zeuzem et al. (2004) investigated the efficacy of 1.5 mg/kg of pegylated interferon-alpha once weekly plus 800–1400 mg ribavirin (based on body weight) in HCV-2 (n=42) and HCV-3 (n=182) infected patients for 24 weeks. Patients infected with HCV-2 had higher SVR than patients infected with HCV-3. Baseline viremia ($p=0.020$), treatment duration greater than 16 weeks ($p<0.001$) and steatosis ($<5\%$, $p=0.015$) were significant independent predictors of SVR. Adverse events resulted in discontinuation in 5% and dose reduction in 22% of patients. The authors concluded that the treatment for 24 weeks with peginterferon alfa and ribavirin could be sufficient in HCV 2 or 3 infected patients. However, the high viral load and hepatic steatosis are significantly associated with reduced SVR in HCV-3 infected patients.

Patients who experience a relapse are likely to respond and experience a relapse again with a subsequent course of the same therapy. However, the chance of achieving an SVR in relapsers could be as high as 40%–50% if re-treatment is pursued with more effective therapy. Based on a recent analysis of 624 patients in response to IFN-based therapy, 98% of all relapses occur within the first 12 weeks after cessation of therapy. If this group of patients is to be re-treated, a more effective regimen should be used. Several studies have reported that relapsers after a course of standard IFN monotherapy or of standard IFN/ribavirin combination therapy are candidates for PEG-IFN plus ribavirin. One prospective trial showed an SVR in 42% of patients who, having experienced a relapse previously after being treated with standard IFN and ribavirin, were re-treated subsequently with PEG-IFN and ribavirin for 48 weeks.

Two open-labeled, multicenter studies evaluated the potential benefits of extending treatment from 48 to 72 weeks with peginterferon-alpha 2a plus ribavirin. In a partially randomized, open-label, parallel-group, multicenter study (Sanchez–Tapias, et al., 2006), a total of 510 HIV-negative treatment-naïve patients received subcutaneous peginterferon-alfa2a 180 µg/week plus oral ribavirin 800 mg/day during the treatment phase of the study. To identify subjects with a rapid virologic response (RVR), all patients were tested for HCV RNA after four weeks of treatment using a qualitative polymerase chain reaction assay with a limit of detection of 50 IU/mL. RVR was defined as undetectable HCV-RNA levels at week four of therapy. After four weeks of therapy, 326 patients who still had detectable HCV RNA were randomly assigned to continue treatment for a total of 48 weeks (the standard duration of therapy for individuals with genotype 1 HCV; n=165) or 72 weeks (n=161). The 184 patients with undetectable HCV RNA at week four were allocated into two groups on the basis of genotype and baseline viral load, and were treated for a total of 24 weeks (the standard duration for individuals with genotypes 2 or 3) or 48 weeks. The end-of-treatment response rates were similar in the week four HCV RNA detectable patients whether they were treated for a total of 48 or 72 weeks (about 60%). However, the SVR rate (measured 24 weeks after the end of therapy) was higher for those receiving treatment for 72 weeks compared with 48 weeks (45% vs. 32%; $p=0.01$). Looking only at the genotype 1 patients with detectable HCV RNA at week four, 44% of those treated for 72 weeks achieved SVR, compared to 28% of those treated for 48 weeks ($p=0.003$). Among the week four HCV RNA undetectable patients, SVR rates were 79% in the arm treated for 24 weeks (i.e., genotype 2 or 3) and 64% in the arm treated for 48 weeks (i.e., genotype 1). The incidence of adverse events was similar in all groups. Among the week four HCV RNA detectable patients, treatment discontinuation was more frequent in the arm treated for 72 weeks compared to 48 weeks (36% vs. 18%; $p=0.0004$). The study shows that the extension of treatment with peginterferon-alfa2a plus ribavirin from 48 to 72 weeks increases the rate of SVR in patients with detectable viremia at week four of treatment. This study adds to the evidence that tailoring hepatitis C treatment on the basis of early virological response can produce improved outcomes while minimizing unnecessary side effects. However, more research is needed to determine optimal treatment duration for HIV/HCV coinfecting individuals.

In a randomized prospective trial (Berg, et al., 2006), researchers evaluated the extended treatment duration from 48 to 72 weeks in 455 HCV-positive, treatment-naïve patients. Subjects received weekly subcutaneous pegylated interferon-alpha-2a (180 µg) plus daily oral ribavirin (800 mg) for either 48 weeks or 72 weeks. Viral assays were performed at 4, 12, and 24 weeks and at the end of treatment to assess response. Patients without substantial drops ($>\log 2$) in viral count at 24 weeks were considered to be nonresponders. Discontinuation rates were higher in the 72-week group than in the 48-week group (41% versus 24%, respectively). SVR was achieved in 54% of patients who received 72-week therapy and in 53% of those who received 48-week therapy. Patients with undetectable viral loads at weeks 4 and 12 had an excellent SVR rate regardless of treatment duration. However, patients with detectable viral loads, especially if counts were < 6000 IU/mL, benefited from a

longer duration of therapy. In these patients, SVR occurred in 29% of the 72-week group versus 17% of the 48-week group (p=0.04). Results showed that SVR rates in genotype 1 HCV-positive patients generally do not improve with extended treatment duration, although a certain subgroup of patients with initial slow responses to therapy might benefit from extended treatment. High discontinuation rates in the 72-week group and findings based on subgroup analysis require additional safety and efficacy studies for the extended treatment duration with peginterferon alpha.

Ongoing Studies

Currently, pegylated interferon alfa-2b is in pending approval investigational stage for the treatment of malignant melanoma, as monotherapy or in combination with other agents. Results of Phase III trial published in *The Lancet* (2008) showed that long-term treatment with pegylated interferon alfa-2b in stage III melanoma patients had a significant and sustained impact on relapse-free survival (RFS). At 3.8 years median follow up, risk of recurrence or death was reduced by 18 percent in pegylated interferon alfa-2b arm compared with observation. The four-year RFS rate was 46 percent vs. 39 percent in observation arm.

In addition, pegylated interferon alfa-2b is in Phase III for the prevention of recurrent hepatitis C infection and allograft hepatitis following liver transplant in patients, in combination with ribavirin, and for the treatment of liver fibrosis or cirrhosis following chronic hepatitis C in patients who failed to respond to previous treatment with an alfa interferon plus ribavirin.

Adverse Drug Reactions/Drug Interactions/Precautions

Use of ribavirin plus peginterferon alfa-2b combination therapy is contraindicated in patients with chronic hepatitis C virus (HCV) infection, with or without HIV coinfection, who demonstrate hepatic decompensation prior to or during treatment. Ribavirin may cause birth defects and/or death of the unborn child. Extreme care must be taken to avoid pregnancy in female patients and in female partners of male patients. Ribavirin causes hemolytic anemia. The anemia associated with ribavirin therapy may result in a worsening of cardiac disease.

The adverse effect profile of peginterferon alfa-2b is similar to interferon alfa-2b. The main adverse events associated with peginterferon alfa-2b are flu-like symptoms, asthenia, decreased neutrophil and platelet counts, psychiatric symptoms, and thyroid-stimulating hormone abnormalities.

Coding/Billing Information

Note: This section is not in use.

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Policy History

Pre-Merger Organizations	Last Review Date	Policy Number	Title
CIGNA HealthCare Great-West Healthcare	1/15/2009	6004	Peginterferon Alfa-2b (PEG Intron®)

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