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Peginterferon Prior Authorization Criteria

- Program may be implemented with the following options
- option 1) Prior authorization through preferred product
 - option 2) Step therapy through preferred product
 - option 3) Prior authorization for all products (no product preference)

For BlueCross BlueShield of New Mexico and BlueCross BlueShield of Oklahoma, Option 1 (prior authorization through preferred peginterferon product Pegasys) will apply. For BlueCross BlueShield of Texas and BlueCross BlueShield of Illinois, Option 3 (prior authorization for all products with no product preference) will apply.

Brand	Generic	Dosage Form
Pegasys®	peginterferon alfa-2a	injection
PegIntron®	peginterferon alfa-2b	injection

PROGRAM OBJECTIVES

The intent of the prior authorization (PA) criteria for the peginterferons is to ensure appropriate selection of patients for treatment and for duration of therapy according to product labeling and/or clinical studies and/or guidelines and when criteria are met, approve for use of the more cost-effective, preferred agent, Pegasys (option 1). The PA criteria may also be applied to both peginterferon agents without product preference (option 3) or as step therapy, encouraging the use of the more cost-effective preferred agent before nonpreferred products (option 2).

The manual PA process limits approvals for a specified duration of therapy depending on diagnosis. Proper duration of treatment is 12 continuous months for infection with Hepatitis C virus (HCV) genotype 1, 4, 5, or 6 if there is a response to therapy at 12 weeks, and six continuous months for genotype 2 and 3 which may be extended to 12 continuous months if there is evidence of cirrhosis, high viral load, or delayed response. There is evidence that patients considered slow responders may benefit from a 72 week course of therapy. To accommodate this extended length of therapy and to allow for possible disruptions in therapy, the PA process will allow for up to 24 months of therapy for a diagnosis of HCV if the patient has confirmed HCV infection. The recommended duration of treatment with interferon is 16 weeks for Hepatitis B 'e' antigen (HBeAg) positive HBV and 12 months for HBeAg negative HBV if the patient has confirmed HBV infection. To accommodate the 12 month treatment duration and allow for possible disruptions in therapy, the PA process will allow up to 18 months of peginterferon therapy for a diagnosis of Hepatitis B virus (HBV). When prescribed for treatment of a cancerous or precancerous condition, peginterferon may be approved indefinitely.

The intent of the step therapy criteria is to direct use through the preferred agent and allows use of nonpreferred peginterferon if the patient has tried and failed, has an allergy, contraindication, or intolerance to the preferred agent or if the prescriber submits evidence in support of therapy with the nonpreferred agent.

PROGRAM FUNCTIONALITY

Electronic Edit

Prior Authorization [applies to option 1 and 3]

The overall process for a prior authorization will not allow the targeted drugs to adjudicate through the claims system. When a patient requests a targeted drug listed in Table 1 below, the system will reject the claim with the message indicating that prior authorization is necessary. The Prior Authorization (PA) Criteria for Approval would then be applied to requests submitted by the patient's practitioner for evaluation.

Table 1: Targeted Agents for Peginterferon Prior Authorization

Agent	GPI (multisource code)
Pegasys (peginterferon alfa-2a)	
180 mcg/ml injection	12353060056420 (M, N, O, or Y)
PegIntron (peginterferon alfa-2b)	
50 mcg/0.5 ml injection	12353060106410 (M, N, O, or Y)
80 mcg/0.5 ml injection	12353060106416 (M, N, O, or Y)
120 mcg/0.5 ml injection	12353060106424 (M, N, O, or Y)
150 mcg/0.5 ml injection	12353060106430 (M, N, O, or Y)

Step Therapy [applies to option 2 only]

The electronic step edit for the peginterferon agents will allow automatic payment of the preferred agent, Pegasys. The step edit will allow automatic payment of the nonpreferred agent, PegIntron, if the patient is being treated with PegIntron (claims history for the patient indicates a claim for PegIntron in the previous 90 days) or if the patient has tried Pegasys and is switching to PegIntron (claims history for the patient indicates a claim for Pegasys in the previous 90 days). The system searches for a claim with a days supply that begins or ends in the past 90 days. For claims with a 30 day supply the system would be able to identify a claim processed for payment between 1 and 120 days prior to the new claim. For claims that are dispensed as an extended days supply (90 days), the system would identify a claim processed between 1 and 180 days. Claims for PegIntron, not meeting the preferred agent edit, would be reviewed through a manual prior authorization process.

Table 2: Summary of Peginterferon Step Therapy

Targeted Agent	PegIntron
Is auto-grandfathering implemented? (with look-back time frame)	Yes (90 day look-back ^a)
Prerequisite Agent	Pegasys
Number of prerequisites required	1
Prerequisite look-back time frame	90 days ^a
Age-related edit?	No
Additional comments	

a - The system searches for a claim with a days supply that begins or ends in the past 90 days. For claims with a 30-day supply the system would be able to identify a claim processed for payment between 1 and 120 days prior to the new claim. For claims that are dispensed as an extended days supply (90 days), the system would identify a claim processed between 1 and 180 days.

Table 3: Details of Peginterferon Step Therapy

Targeted Agents	GPI (multisource code)	Prior Agents	GPI (multisource code)	Look-back Time frames
PegIntron	1235306005**** (M, N, O, or Y)	For Prerequisites Pegasys	1235306010**** (M, N, O, or Y)	Prerequisite look-back time frame: 90 days ^a
		For Auto-grandfathering PegIntron	1235306005**** (M, N, O, or Y)	Auto-grandfathering look-back time frame: 90 days ^a

a - The system searches for a claim with a days supply that begins or ends in the past 90 days. For claims with a 30-day supply the system would be able to identify a claim processed for payment between 1 and 120 days prior to the new claim. For claims that are dispensed as an extended days supply (90 days), the system would identify a claim processed between 1 and 180 days.

If the patient does not meet the step therapy criteria, then the system will reject with the message indicating that prior authorization is necessary. The *Prior Authorization (PA) Criteria for Approval* would then be applied to requests submitted by the patient's practitioner for evaluation.

Prior Authorization Criteria for Approval

The Prior Authorization (PA) Criteria for Approval provide the manual review process for all claims for targeted agents in this PA program.

**Option 1: through preferred agent, Pegasys
Pegasys and PegIntron**

Initial Evaluation

1. Has the patient been previously approved for peginterferon through the Prime Therapeutics prior authorization approval process?
If yes, see renewal criteria. If no, continue to 2.
2. What is the diagnosis?
 - a. A cancerous or pre-cancerous condition
 - b. Chronic hepatitis B virus (HBV) infection
 - c. Acute or chronic hepatitis C (HCV) infection
 - d. Other
 If a, continue to 8. If b, continue to 3. If c, continue to 5. If d, deny.
3. Has the patient previously received a course of interferon or peginterferon therapy?
If yes, deny. If no, continue to 4.
4. Has diagnosis of chronic HBV been confirmed by detection of serologic markers for the infection?
If yes, continue to 8. If no, deny.
5. Has the patient previously received a course of interferon or peginterferon therapy?
If yes, deny. If no, continue to 6.
6. Has the diagnosis of HCV been confirmed by detection of serologic markers for the infection?
If yes, continue to 7. If no, deny.

7. Has peginterferon been prescribed as a maintenance dose for HCV?
If yes, deny. If no, continue to 8.

8. Is the request for the *preferred* peginterferon agent, Pegasys?
If yes, approve for a duration based on diagnosis:
 - a. A cancerous or pre-cancerous condition - indefinitely
 - b. Chronic hepatitis B virus (HBV) infection - 18 months (or the remainder of 18 months if the patient is already receiving a course of therapy)
 - c. Acute or chronic hepatitis C (HCV) infection – initiation of a course of therapy – 6 months
 - d. Acute or chronic hepatitis C (HCV) infection – continuation to finish a treatment course - remainder of course, up to 24 months
 If no, continue to 9.

9. Is the patient currently being treated with the *nonpreferred* agent, PegIntron?
If yes, approve for a duration based on diagnosis:
 - a. A cancerous or pre-cancerous condition - indefinitely
 - b. Chronic hepatitis B virus (HBV) infection - remainder of 18 months
 - c. Acute or chronic hepatitis C (HCV) infection – remainder of 24 months
 If no, continue to 10.

10. Does the patient have a history of a trial and failure of, or contraindication to, intolerance of, or allergy to the *preferred* agent, Pegasys?
If yes, approve for a duration based on diagnosis:
 - a. A cancerous or pre-cancerous condition - indefinitely
 - b. Chronic hepatitis B virus (HBV) infection - 18 months (or the remainder of 18 months if the patient is already receiving a course of therapy)
 - c. Acute or chronic hepatitis C (HCV) infection – initiation of a course of therapy – 6 months
 - d. Acute or chronic hepatitis C (HCV) infection – continuation to finish a treatment course - remainder of course, up to 24 months
 If no, continue to 11.

11. Has the prescriber submitted and the pharmacist reviewed documentation in support of therapy with the *nonpreferred* agent, PegIntron?
If yes, pharmacist must review and may approve for an appropriate duration of therapy based on review of information provided. If no, deny.

Renewal Evaluation

1. Has the patient been previously approved for peginterferon through the Prime Therapeutics prior authorization approval process?
If yes, continue to 2. If no, see initial criteria.

2. What is the diagnosis?
 - a. A cancerous or pre-cancerous condition
 - b. Chronic hepatitis B virus (HBV) infection
 - c. Acute or chronic hepatitis C (HCV) infection
 - d. Other
 If a, continue to 5. If b, continue to 3. If c, continue to 4. If d, deny.

3. Has the patient received an 18 month course of peginterferon therapy?
If yes, deny. If no, continue to 5.

4. Has the HCV RNA level at or before 6 months (24 weeks) of therapy become negative or decreased by at least two log₁₀ units (such as from 2 million IU to 20,000 IU or less)?
If yes, continue to 5. If no, deny.

5. Is the request for the *preferred* peginterferon agent, Pegasys?
If yes, approve for a duration based on diagnosis:
 - a. A cancerous or pre-cancerous condition - indefinitely
 - b. Chronic hepatitis B virus (HBV) infection - remainder of 18 months
 - c. Acute or chronic hepatitis C (HCV) infection – remainder of 24 months
 If no, continue to 6.

6. Is the patient currently being treated with the *nonpreferred* agent, PegIntron?
If yes, approve for a duration based on diagnosis:
 - a. A cancerous or pre-cancerous condition - indefinitely
 - b. Chronic hepatitis B virus (HBV) infection - remainder of 18 months
 - c. Acute or chronic hepatitis C (HCV) infection – remainder of 24 months
 If no, continue to 7.

7. Does the patient have a history of a trial and failure of, or contraindication to, intolerance of, or allergy to the *preferred* agent, Pegasys?
If yes, approve for a duration based on diagnosis:
 - a. A cancerous or pre-cancerous condition - indefinitely
 - b. Chronic hepatitis B virus (HBV) infection - remainder of 18 months
 - c. Acute or chronic hepatitis C (HCV) infection – remainder of 24 months
 If no, continue to 11.

8. Has the prescriber submitted and the pharmacist reviewed documentation in support of therapy with the *nonpreferred* agent, PegIntron?
If yes, pharmacist must review and may approve for an appropriate duration of therapy based on review of information provided. If no, deny.

**Option 2: Step Therapy through preferred, Pegasys
PegIntron**

Initial and Renewal Evaluation

1. Is the patient currently being treated with the nonpreferred agent, PegIntron?
If yes, approve for 12 months. If no, continue to 2.

2. Does the patient's medication history indicate previous use of Pegasys?
If yes, approve for 12 months. If no, continue to 3.

3. Does the patient have an allergy, contraindication, or intolerance to the preferred agent, Pegasys?
If yes, approve for 12 months. If no, continue to 4.

4. Has the prescriber provided and the pharmacist reviewed evidence in support of the use of the requested nonpreferred peginterferon product for the treatment of the intended diagnosis?
If yes, pharmacist must review and may approve for 12 months. If no, deny.

**Option 3: Prior Authorization all products-no product preference
Pegasys and PegIntron**

Initial Evaluation

1. Has the patient been previously approved for peginterferon through the Prime Therapeutics prior authorization approval process?
If yes, see renewal criteria. If no, continue to 2.
2. What is the diagnosis?
 - a. A cancerous or pre-cancerous condition
 - b. Chronic hepatitis B virus (HBV) infection
 - c. Acute or chronic hepatitis C (HCV) infection
 - d. OtherIf a, approve indefinitely. If b, continue to 3. If c, continue to 5. If d, deny.
3. Has the patient previously received a course of interferon or peginterferon therapy?
If yes, deny. If no, continue to 4.
4. Has diagnosis of chronic HBV been confirmed by detection of serologic markers for the infection?
If yes, approve for 18 months (or the remainder of 18 months if the patient is already receiving a course of therapy). If no, deny.
5. Has the patient previously received a course of interferon or peginterferon therapy?
If yes, deny. If no, continue to 6.
6. Has the diagnosis of HCV been confirmed by detection of serologic markers for the infection?
If yes, continue to 7. If no, deny.
7. Has peginterferon been prescribed as a maintenance dose for HCV?
If yes, deny. If no, continue to 8.
8. Is peginterferon being continued to finish a treatment course (member is currently receiving peginterferon)?
If yes, approve for remainder of course, up to 24 months. If no, approve for 6 months.

Renewal Evaluation

1. Has the patient been previously approved for peginterferon through the Prime Therapeutics prior authorization approval process?
If yes, continue to 2. If no, see initial criteria.
2. What is the diagnosis?
 - a. A cancerous or pre-cancerous condition
 - b. Chronic hepatitis B virus (HBV) infection
 - c. Acute or chronic hepatitis C (HCV) infection
 - d. OtherIf a, approve indefinitely. If b, continue to 3. If c, continue to 4. If d, deny.
3. Has the patient received an 18 month course of peginterferon therapy?
If yes, deny. If no, approve for remainder of 18 months.
4. Has the HCV RNA level at or before 6 months (24 weeks) of therapy become negative or decreased by at least two log₁₀ units (such as from 2 million IU to 20,000 IU or less)?
If yes, approve for the remainder of 24 months. If no, deny.

CLINICAL RATIONALE

This prior authorization (PA) program for the peginterferons is to ensure appropriate selection of patients for treatment and for duration of therapy according to product labeling and/or clinical studies and/or guidelines. The PA *through preferred* criteria applies the PA criteria for approval to requests for the peginterferon products and details the PA for approval of the preferred product, Pegasys, for patients initiating therapy with peginterferon. [Patients who have been receiving therapy with PegIntron will be approved for continued use of PegIntron for the entire course of therapy.] The intent of the step therapy criteria is to direct use through the preferred agent Pegasys and allows use of nonpreferred peginterferon PegIntron if the patient has tried and failed, has an allergy, contraindication, or intolerance to the preferred agent or if the prescriber submits evidence in support of therapy with the nonpreferred agent

Pegasys is interferon alpha 2a covalently bound to a single branched bis-monomethoxy polyethylene glycol (PEG) chain whereas PegIntron is interferon alpha 2b covalently bound to PEG monomethoxy ether. Interferon Alpha 2a and 2b are both 165 amino acids and 19,000 daltons weight. They differ only at position 23 in the amino acid sequence with an alpha 2a possessing lysine and alpha 2b possessing an arginine group at this position. The importance, if any, of the single amino acid difference between interferon alpha 2a and 2b has not been established and it remains to be elucidated whether clinically important differences in therapeutic and /or toxicologic profiles exist. [See Chapter 1.10D Antivirals Hepatitis C Agents]³

The two agents, Pegasys and PegIntron have been compared in a head-to-head trial evaluating two doses of PegIntron plus ribavirin and Pegasys plus ribavirin for rate of sustained virologic response and for safety.⁴ Patients (N=3,070) who had HCV genotype 1 infection and who had not previously been treated were randomly assigned to 48 weeks of treatment with one of three regimens: PegIntron at a standard dose of 1.5 mcg per kilogram of body weight per week or a low dose of 1.0 mcg per kilogram per week, plus ribavirin at a dose of 800 mg to 1400 mg per day, or Pegasys at a dose of 180 mcg per week plus ribavirin 1000 mg to 1200 mg per day. At study end, the rates of sustained virologic response and tolerability did not differ significantly between the two peginterferon/ribavirin regimens or between the two doses of PegIntron. Rates of virologic response were 39.8% with standard dose PegIntron, 38.0% with low-dose PegIntron, and 40.9% with Pegasys (p=0.02 for standard versus low dose for PegIntron; p=0.57 for standard dose PegIntron versus Pegasys). Relapse rates were 23.5% (95% confidence interval [CI], 19.9 to 27.2) for standard-dose PegIntron, 20% (95% CI, 16.4 to 23.6) for low-dose PegIntron, and 31.5% (95% CI, 27.9 to 35.2) for Pegasys. The safety profile was similar among the three groups; serious adverse events were observed in 8.6% to 11.7% of patients. Among the patients with undetectable HCV RNA levels at weeks 4 and 12, a sustained virologic response was achieved in 86.2% and 78.7%, respectively.⁴

Proper selection is determined by Food and Drug Administration (FDA) approved label indications; Hepatitis B virus (HBV) infection or Hepatitis C virus (HCV) infection with or without HIV coinfection.^{1,2} The PA criteria for the peginterferons will not differentiate between the two alpha peginterferon agents based on FDA indications. None of the available guidelines differentiate one peginterferon from the other.³ Although peginterferon alpha-2b is not labeled for treatment of hepatitis B and hepatitis B plus HIV co-infection, controlled trials show that it is effective in these disease states.³ Treatment for oncology diagnoses will also be approved although there are few studies evaluating peginterferon in oncology. Available studies indicate similar efficacy between the pegylated and nonpegylated interferons for cancer indications.⁵⁻⁷ However, some state statutes require automatic approval of chemotherapeutic agents for patients with cancerous or pre-cancerous conditions. A Prime Therapeutics data analysis of claims (April 2008 through December 2008) indicates 1.9% of peginterferon is used for a cancer diagnosis.⁸

The diagnosis of HBV is based on the presence of serological markers in the blood; Hepatitis B viral DNA (HBV DNA), hepatitis B surface antigen (HBsAg) or hepatitis B 'e' antigen (HBeAg).^{13,23} The hepatitis B 'e' antigen is an indicator of viral replication but some variant forms of the virus do

not express HBeAg. The PA criteria will approve peginterferon therapy if there are serologic markers confirming HVB infection.²³ Quantification of viral load will not be required.¹⁰

Patients who react positively to enzyme immunoassay for antibody to HCV or HCV RNA, and have compensated liver disease are potential candidates for peginterferon therapy.⁹⁻¹² Antiviral therapy is not recommended routinely for patients with decompensated liver disease, patients with a history of severe, uncontrolled psychiatric disorder, or patients with severe hematologic cytopenia.¹⁰ The PA criteria for the peginterferons will approve an initial 6 months of therapy if testing confirms HCV infection.^{14,23} Although liver biopsy has been regarded as the standard for defining liver disease status, it is not without risks including pain, bleeding, or perforation of other organs.¹² The procedure is subject to sampling error, requires special expertise for interpreting the histopathology, adds cost to medical care, and is anxiety-provoking for the patient.¹² A liver biopsy may not be necessary in persons infected with genotypes 2 or 3 HCV. The PA criteria for the peginterferons will not require that a biopsy be performed.¹²

Current treatment guidelines^{9,10,12} recommend a quantitative serum HCV RNA be performed at the initiation of or shortly before, treatment and also at week 12 of therapy. Persons who achieve a sustained virologic response (SVR) almost always have a dramatic earlier reduction in the HCV RNA level defined often as a 2-log drop or loss of HCV RNA 12 weeks into therapy.^{10,12} In the absence of this type of response, the likelihood of an SVR is 0-3%. Peginterferon therapy will be approved beyond the initial 6 months only if a second serum HCV RNA level shows a 2-log drop.²³

Proper duration of treatment is 12 continuous months for infection with HCV genotype 1, 4, 5, or 6 if there is a response to therapy at 12 weeks and six continuous months for genotype 2 and 3 which may be extended to 12 continuous months if there is evidence of cirrhosis, high viral load, or delayed response (response at 24 weeks versus 12 weeks).^{9,11} There is evidence that patients considered slow responders (positive HCV RNA after 12 weeks of treatment but HCV RNA negative after 24 weeks) may benefit from a 72 week course of therapy.^{14,15} To accommodate this extended length of therapy and to allow for possible disruptions in therapy, the PA process will allow for up to 24 months of therapy for a diagnosis of HCV. The value of continuation of therapy beyond 24 months is currently unproven and considered investigational or experimental.²³

The possibility of a shorter course of peginterferon therapy for patients infected with genotype 2 or 3 HCV has been investigated in several clinical trials.¹⁶⁻¹⁸ In one, randomized, open-label study (n=283), patients with HCV genotype 2 or 3 were treated with either 12 or 24 weeks of peginterferon alfa-2b.¹⁶ If a patient had a virologic response to treatment at week 4, the patient was given treatment for 12 weeks. If no virological response was seen at week 4, the patient was given treatment for 24 weeks. The shorter course of therapy over 12 weeks was determined to be as effective as a 24-week course in patients who have a response to treatment at 4 weeks.¹⁶ Another study of similar design (N=153) including patients with HCV genotype 2 or 3 found that a course of 16 weeks is as effective as a 24-week course in patients who have a response to treatment at 4 weeks.¹⁷ However, in a study by Shiffman et al, which randomized 1,469 patients with HCV genotype 2 or 3 to receive 180 micrograms of peginterferon alfa-2a once weekly, plus 800 milligrams of ribavirin daily, for either 16 weeks or 24 weeks failed to demonstrate that the 16-week regimen was noninferior to the 24-week regimen.¹⁸ The sustained virologic response rate was significantly lower in patients treated for 16 weeks than in patients treated for 24 weeks (62 percent versus 70 percent, $p < 0.001$).¹⁷ Rate of relapse was significantly greater in the 16-week group (31 percent versus 18 percent in the 24-week group, $p < 0.001$).¹⁸ Among patients with a rapid virologic response (no detectable HCV RNA) at week 4, sustained virologic response rates were 79 percent in the 16-week group and 85 percent in the 24-week group ($p = 0.02$).¹⁸ In a phase III trial by Lagging et al, 382 patients with infected with genotype 2 and 3 HCV were randomized to 12 or 24 weeks of therapy with peginterferon alfa-2a and ribivirin.¹⁹ In this trial, 12 weeks of therapy was inferior to 24 weeks in the intent-to-treat population (SRV rates: 59% versus 78%, $p < 0.0001$) and in the subgroups of patients infected with genotype 2 (56% versus 82%, $p = 0.0006$) or genotype 3 (58% versus 78%, $p = 0.0015$).¹⁹

Because of conflicting results in these shorter course studies, the PA criteria for the peginterferons will not restrict the duration of therapy for patients with HCV genotype 2 or 3 who demonstrate a rapid virologic response to a shorter course.

Patients who achieve undetectable HCV RNA during and at the end of therapy but relapse are likely to respond and relapse again with subsequent treatment with the same therapy.^{10,11} Longer duration of therapy with peginterferon or peginterferon plus ribavirin in patients experiencing relapse is of unproven efficacy.^{10,11} Nonresponders to therapy have been considered for treatment with long-term maintenance therapy which may possibly slow the development of fibrosis and limit the progression of cirrhosis to end-stage liver disease or hepatocellular carcinoma.¹⁰ There are currently several trials in progress evaluating the long-term effect of low-dose peginterferon for patients with chronic HCV and advanced fibrosis. One study, HALT-C (Hepatitis C Antiviral Long-Term Treatment against Cirrhosis), has been completed and published. In this randomized, controlled trial (n=1050) of peginterferon alfa-2a, a low dose (90 mcg/week) for 3.5 years was compared with no treatment in patients with chronic HCV and advanced fibrosis who had not previously responded to therapy with peginterferon plus ribavirin.²⁰ The primary endpoint was progression of liver disease, as indicated by death, hepatocellular carcinoma, hepatic decompensation, or for those with bridging fibrosis at baseline, an increase in the Ishak fibrosis score of two or more points. After 3.5 years of treatment, no significant differences were apparent between the groups in the rate of any primary outcome (34.1% in the treatment group versus 33.8% in the control group [Hazard Ratio 1.01; 95% CI, 0.81 to 1.27;p=0.90]). Fifty-three patients (5%) died, 31 in the treatment group and 22 in the control group (p=0.18).¹⁹ There was a significant difference in mortality between the treatment and control groups among patients with noncirrhotic fibrosis (5% versus 1.9%, p=0.04), but not among patients with cirrhosis (9.1% and 8.4%; p=0.93).²⁰ The percentage of patients with at least one serious adverse event was 38.6% in the treatment group and 31.8% in the control group (p=0.07).²⁰ Dose modifications for adverse events were frequent; by year 3.5, only 58.9% of patients who were still in the study and had not had a clinical outcome were receiving the full 90 mcg treatment dose of peginterferon.²⁰ Treatment guidelines from the American Association for the Study of Liver Diseases (AASLD 2009) do not recommend maintenance therapy for patients with bridging fibrosis or cirrhosis who have failed a prior course of peginterferon and ribavirin.¹²

The AASLD 2009 guideline for the treatment of HBV recommends initiation of treatment with any of the seven approved antiviral medications but peginterferon, tenofovir, or entecavir are preferred.²¹ Advantages of peginterferon include a finite duration of treatment, a more durable response, and lack of resistant mutants.^{21,22} The AASLD 2009 guideline for HBV recommends duration of treatment with standard interferon for 16 weeks for HBeAg positive HBV and 48 weeks for peginterferon.²¹ The recommended treatment duration for HBeAg-negative chronic hepatitis B is 48 weeks for both standard and peginterferon.²¹ The European Association for the Study of the Liver (EASL) practice guideline (2009) also suggests peginterferon for 48 weeks for both HBeAg positive HBV and HBeAg negative HBV.²² To accommodate the 12 month treatment duration and allow for possible disruptions in therapy, the PA process will allow up to 18 months of peginterferon therapy for a diagnosis of HBV. Patients who fail to respond to interferon therapy may be retreated with lamivudine or adefovir.²¹ There is no renewal of therapy criteria beyond initial 18 month PA approval. The decision to retreat HBV infected patients with peginterferon will be referred to the health plan for determination of coverage.

FDA APPROVED INDICATIONS^{1,2}

Pegasys¹

Pegasys (peginterferon alfa-2a alone or in combination with Copegus[®] (ribavirin), is indicated for the treatment of adults with chronic hepatitis C virus infection who have compensated liver disease and have not been previously treated with interferon alpha. Patients in whom efficacy has been demonstrated included patients with compensated liver disease and histological evidence of cirrhosis (Child-Pugh class A) and patients with HIV disease that is clinically stable (e.g., antiretroviral therapy not required or receiving stable antiretroviral therapy).

Pegasys is indicated for the treatment of adult patients with HBeAg positive and HBeAg negative chronic hepatitis B who have compensated liver disease and evidence of viral replication and liver inflammation.

PegIntron²

PegIntronTM (peginterferon alfa-2b), is indicated for:

- Combination therapy with ribavirin: Chronic Hepatitis C (CHC) in patients ≥ 3 years with compensated liver disease.
Patients with the following characteristics are less likely to benefit from re-treatment after failing a course of therapy: previous nonresponse, previous pegylated interferon treatment, significant bridging fibrosis or cirrhosis, and genotype 1 infection.
- Monotherapy: CHC in patients (≥ 18 years) with compensated liver disease previously untreated with interferon alpha.

Table 4: FDA-Labeled Indications for Peginterferons^{1,2}

Available Products	INDICATIONS			
	Hepatitis C	Hepatitis C in combination with ribavirin	Hepatitis B	HCV + HIV co infection
Peginterferon alfa-2a (Pegasys [®])	✓	✓ ^a	✓	✓
Peginterferon alfa-2b (PegIntron TM)	✓ (>18 yr)	✓ (≥ 3 yr)		

^a Efficacy was demonstrated in patients with compensated liver disease and histological evidence of cirrhosis and patients with HIV disease that is clinically stable.

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