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Peginterferon Prior Authorization Criteria

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

FDA APPROVED INDICATIONS

Pegasys®¹

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.

PegIntron®²

PegIntron® (peginterferon alfa-2b), is indicated for use alone or in combination with Rebetol® for the treatment of chronic hepatitis C in patients with compensated liver disease who have not been previously treated with interferon alfa and who are 18 years of age or older.

Table 1. FDA Labeled Indications for PegInterferon Alfa Agents^{1,2}

Available Products	INDICATIONS			
	Hepatitis C	Hepatitis C in combination with ribavirin	Hepatitis B	HCV + HIV co infection
Peginterferon alfa-2a (Pegasys®)	✓	✓*	✓†	✓‡
Peginterferon alfa-2b (PegIntron®)	✓	✓		

* Efficacy was demonstrated in patients with compensated liver disease and histological evidence of cirrhosis and patients with HIV disease that is clinically stable.
† Indication for hepatitis B was recently approved (May 2005) for peginterferon alfa-2a by the FDA.
‡ Indication for chronic hepatitis C with HIV co infection was recently approved (February 2005) for peginterferon alfa-2a by the FDA.

RATIONALE FOR PRIOR AUTHORIZATION

The intent of the Prior Authorization (PA) criteria for peginterferon therapy is to ensure that patients are appropriately selected and treated for an appropriate duration of therapy according to parameters defined in product labeling and/or clinical evidence and/or guidelines. 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 alfa peginterferon agents based on FDA indications. 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.^{3,4} However, some state statutes require automatic approval of chemotherapeutic agents for patients with cancerous or pre-cancerous conditions.

Hepatitis B

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).⁷ 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 HBV infection.¹¹ Quantification of viral load will not be required.⁷

The American Association for the Study of Liver Diseases (AASLD) guidelines for the treatment of HBV recommends interferon alfa, lamivudine, or adefovir as initial therapy.⁹ Advantages of interferon include a finite duration of treatment, a more durable response, and lack of resistant mutants. The recommended duration of treatment with interferon is 16 weeks for HBeAg positive HBV and 12 months for HBeAg negative HBV.⁹ 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.¹¹ Patients who fail to respond to interferon therapy may be retreated with lamivudine or adefovir.⁹ 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.

Hepatitis C

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.^{5,6} 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.⁶ The PA criteria for the peginterferons will approve an initial 6 months of therapy if testing confirms HCV infection.¹¹

Current treatment guidelines^{5,6,10} 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.^{6,10} 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.¹¹

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).⁵ There is evidence that patient's 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.⁸ 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.¹¹ The value of continuation of therapy beyond 24 months is currently unproven and considered investigational or experimental.¹¹

Overall, an SVR can be achieved by retreatment with peginterferon and ribavirin in 20% to 40% of persons who failed to respond to interferon alfa monotherapy and in about 10% who failed to respond to interferon alfa and ribavirin.^{5,6,10} Decisions regarding re-treatment should be based on:

- (1) previous type of response,
- (2) the previous therapy and the difference in potency of the new therapy,
- (3) the severity of the underlying liver disease,
- (4) viral genotype and other predictive factors for response, and
- (5) tolerance of previous therapy and adherence.

Knowledge of the severity of the underlying liver disease is important in recommending re-treatment. Patients with advanced fibrosis or cirrhosis have an increased risk of hepatic decompensation and should be considered for re-treatment, especially if they were originally treated with interferon monotherapy.⁵ Expectations for responsiveness to re-treatment are lower in patients with genotype 1, cirrhosis, high baseline HCV RNA levels, and black ethnicity.⁶ Current AASLD practice guidelines recommend that retreatment with peginterferon plus ribavirin should be considered for nonresponders or relapsers who have significant fibrosis or cirrhosis and who have undergone previous regimens of treatment using non-pegylated interferon.¹⁰ The decision to treat members who have had previous interferon alfa therapy will be referred to the health plan for determination of coverage.

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.⁶ Longer duration of therapy with peginterferon or peginterferon plus ribavirin in patients in patients experiencing relapse is of unproven efficacy.⁶ Nonresponders to peginterferon 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.⁶ There are currently several trials in progress evaluating the long-term effect of low-dose peginterferon for patients with chronic HCV and advanced fibrosis. The results of these trials will determine future recommendations for chronic maintenance therapy in those patients with advanced fibrosis who fail to achieve a sustained virologic response.⁶ Until recommendations can be made on retreatment of relapsing patients and nonresponders to peginterferon therapy, the decision to retreat or continue therapy beyond the initial treatment course will be referred to the health plan for determination of coverage.

PRIOR AUTHORIZATION CRITERIA FOR APPROVAL

Peginterferon

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.

Peginterferon

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, 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.

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Document History

Original Prime Standard approved by UM Committee 02/2005

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