
Prior Authorization DRUG Guidelines

PEGASYS®
(Pegylated interferon (peginterferon) alfa-2a)
Effective Date: 7/28/05
Date Developed: 7/28/05 by C. Wilhelmy MD
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(Archived 1/22/19)

Pegasys is an interferon. Alpha interferons are a family of proteins, produced by nucleated cells, that have antiviral, antiproliferative, and immune-regulating activity. There are 16 known subtypes of alpha interferons. Interferons interact with cells through high affinity cell surface receptors. Following activation, multiple effects can be detected including induction of gene transcription. Inhibits cellular growth, alters the state of cellular differentiation, interferes with oncogene expression, alters cell surface antigen expression, increases phagocytic activity of macrophages, and augments cytotoxicity of lymphocytes for target cells.

Pre-Authorization Criteria:

Pegasys is used for the treatment of chronic hepatitis C (CHC), alone or in combination with ribavirin, in patients with compensated liver disease and histological evidence of cirrhosis (Child-Pugh class A) and patients with clinically-stable HIV disease. It may be prescribed for a maximum of one year.

1. FDA Approved Indications:

- For use alone, or in combination with Copegus (ribavirin), for the treatment of adults with chronic hepatitis C who have compensated liver disease and have not been previously treated with interferon alpha. Patients in whom efficacy was 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.
- Treatment of adult patients with HBeAg positive or HBbeAg negative chronic hepatitis B with compensated liver disease and evidence of viral replication and liver inflammation.

2. Approved Indications and Usage Guidelines:

CHRONIC HEPATITIS C

For all patients

- Patient is 18 years of age or older
- Must be used in combination with ribavirin unless the patient is intolerant to ribavirin or has a contraindication to ribavirin

AND**For previously untreated patients (naïve patients)**

- Diagnosis of chronic hepatitis C confirmed by detectable serum HCV RNA by quantitative assay. Baseline viral load by quantitative assay and genotype are required to determine length of approval and future virologic response.

AND

- Three consecutive elevated ($>2\times$ ULN) transaminases (ALT) at least one month apart (not required for genotype 2 or 3)

OR

- Liver biopsy showing greater than grade 1, stage 1 damage (Stage 3-4 portal or bridging fibrosis, moderate/severe inflammation or necrosis as documented by a Metavir score of greater than or equal to 2, Ishak score of greater than or equal to 3, or necroinflammation (Grade 9-18)). Biopsy results are not needed for genotypes 2 or 3.

OR

- In combination with ribavirin if patient has experienced a relapse after a liver transplantation regardless of prior regimen

OR

- Patient has symptomatic cryoglobulinemia

Non-responders

- In combination with ribavirin if patient has had no prior combination therapy with pegylated interferon and ribavirin

OR

- In combination with ribavirin if patient was a non-responder to the combination of pegylated interferon and ribavirin

Relapsers

- In combination with ribavirin if a patient had an undetectable HCV-RNA level at any time while on treatment for chronic hepatitis C, then developed detectable HCV-RNA levels

Definitions:

Non-responder	Patient never achieved an undetectable viral load during therapy. To qualify for treatment as a nonresponder at least 12 weeks must have elapsed since the first course of therapy.
Breakthrough	Patient's viral load was below the level of detection at one point during therapy but rose to >1000 copies per ml while on continuous therapy.
Relapse	Undetectable viral load increased to >1000 copies/ml after discontinuation of therapy
Sustained virological response (SVR)	HCV RNA negative 24 weeks after cessation of treatment

CHRONIC HEPATITIS B

- Diagnosis of chronic hepatitis B virus infection

AND ONE of the following:

- Two elevated ALT lab values within the past 12 months (≥ 60 IU/L for men, ≥ 38 IU/L for women) and HBV DNA levels $\geq 20,000$ IU/ml
- Patient has cirrhosis
- Patient's liver biopsy showing moderate/severe necroinflammation (Grade 9-18) or significant fibrosis (Stage 3-4)

VCHCP requires that Pegasys be prescribed by a gastroenterologist, or a Hepatitis C or Immunology Clinic physician.

MONITORING PARAMETERS — Standard hematological tests should be performed prior to therapy, at week 2, and periodically. Standard biochemical tests should be performed prior to therapy, at week 4, and periodically. Evaluate for depression and other psychiatric symptoms before and during therapy; baseline eye examination and periodically in patients with baseline disorders; baseline echocardiogram in patients with cardiac disease; serum HCV RNA levels after 12 weeks of treatment

Clinical studies tested as follows: CBC (including hemoglobin, WBC, and platelets) and chemistries (including liver function tests and uric acid) measured at weeks 1, 2, 4, 6, and 8, and then every 4 weeks; TSH measured every 12 weeks

In addition, the following baseline values were used as entrance criteria: Platelet count 90,000/mm³ (as low as 75,000/mm³ in patients with cirrhosis or transition to cirrhosis)

ANC 1500/mm³

Serum creatinine <1.5 times ULN

TSH and T4 within normal limits or adequately controlled

Consider discontinuing treatment if virologic tests indicate no response by week 12.

DOSING: ADULTS Dosing is complex, refer to [Lexi-Comp Online™](#)

DOSING: RENAL IMPAIRMENT

Clcr<50 mL/minute: Use caution; monitor for toxicity

End-stage renal disease requiring hemodialysis: 135 mcg/week; monitor for toxicity

DOSING: HEPATIC IMPAIRMENT — ALT progressively rising above baseline: Decrease dose to 135 mcg/week. If ALT continues to rise or is accompanied by increased bilirubin or hepatic decompensation, discontinue therapy immediately.

DOSAGE FORMS

Injection, solution: 180 mcg/mL (1.2 mL) [contains benzyl alcohol]

Injection, solution [prefilled syringe]: 180 mcg/0.5 mL (0.5 mL) [contains benzyl alcohol; packaged with needles and alcohol swabs]

ADMINISTRATION — SubQ: Administer in the abdomen or thigh. Rotate injection site. Do not use if solution contains particulate matter or is discolored. Discard unused solution. Administration should be done on the same day and at approximately the same time each week.

CONTRAINDICATIONS — Hypersensitivity to polyethylene glycol (PEG), interferon alfa, or any component of the formulation; autoimmune hepatitis; decompensated liver disease in cirrhotic CHC patients monoinfected (Child-Pugh score>6) or coinfecting (Child-Pugh score 6, class B and C) with HIV; neonates and infants

WARNINGS / PRECAUTIONS — Severe acute hypersensitivity reactions have occurred rarely; prompt discontinuation is advised. Use caution with prior cardiovascular disease, endocrine disorders, autoimmune disorders, and pulmonary dysfunction. Discontinue treatment with worsening or persistently severe signs/symptoms of autoimmune, infectious, respiratory, or neuropsychiatric disorders (including depression and/or suicidal thoughts/behavior). Severe psychiatric adverse effects (including depression, suicidal ideation, and suicide attempt) may occur. Avoid use in severe psychiatric disorders; use caution in patients with a history of depression. Patients who experience dizziness, confusion, somnolence or fatigue should use caution when performing tasks which require mental alertness (eg, operating machinery or driving).

Hepatic decompensation and death have been associated with the use of alpha interferons including Pegasys®, in cirrhotic chronic hepatitis C patients; patients coinfecting with HIV and receiving highly active antiretroviral therapy have shown an increased risk. Monitor hepatic function; discontinue if decompensation occurs (Child-Pugh score >6) in

monoinfected patients and (Child-Pugh score 6, class B and C) in patients coinfecting with HIV.

Use caution with renal dysfunction ($\text{Cl}_{\text{cr}} < 50 \text{ mL/minute}$). Patients with renal dysfunction should be monitored for signs/symptoms of toxicity (dosage adjustment required if toxicity occurs). Discontinue if new or worsening ophthalmologic disorders occur including retinal hemorrhages, cotton wool spots, and retinal artery or vein obstruction; visual exams are recommended in these instances, at the initiation of therapy, and periodically during therapy.

Use caution with baseline neutrophil count $< 1500/\text{mm}^3$, platelet count $< 90,000/\text{mm}^3$ or hemoglobin $< 10 \text{ g/dL}$. Discontinue therapy (at least temporarily) if ANC $< 500/\text{mm}^3$ or platelet count $< 25,000/\text{mm}^3$, colitis develops, or if known or suspected pancreatitis develops. Use caution in patients with an increased risk for severe anemia (eg, spherocytosis, history of GI bleeding).

Use caution in geriatric patients. Safety and efficacy have not been established in patients who have failed other alpha interferon therapy, received organ transplants, been infected with hepatitis B, been coinfecting with HIV with a CD4^+ cell count $< 100 \text{ cells/microL}$, or been treated for > 48 weeks. Due to differences in dosage, patients should not change brands of interferon. Safety and efficacy have not been established in children.

DRUG INTERACTIONS — Inhibits CYP1A2 (weak)

ACE inhibitors: Interferons may increase the risk of neutropenia.

Fluorouracil: Concentrations of fluorouracil doubled in patients with gastrointestinal carcinoma who received interferon alfa-2b.

Melphalan: Interferon alpha may decrease the serum concentrations of melphalan.

Prednisone: Prednisone may decrease the therapeutic effects of interferon alpha.

Theophylline: Interferon alfa may decrease the CYP450 metabolism of theophylline.

Warfarin: Interferons may increase the anticoagulant effects of warfarin. Zidovudine: Interferons may decrease the metabolism of zidovudine.

ETHANOL / NUTRITION / HERB INTERACTIONS — Ethanol: Avoid use in patients with hepatitis C virus.

PREGNANCY RISK FACTOR — C; X when used with ribavirin

PATIENT EDUCATION — You may be taught to give yourself the injection if you are willing and able to learn. Blood work will be done before the start of this medicine and during its use. Other tests may be needed depending on your medical history. An eye examination is recommended before starting treatment. Maintain adequate hydration (2-3 L/day of fluids unless instructed to restrict fluid intake). Avoid alcohol. You may experience flu-like syndrome (giving the medicine at bedtime or using acetaminophen may help), nausea and vomiting (frequent small meals, frequent mouth care, sucking lozenges, or chewing gum may help), feeling tired (use caution when driving or engaging in tasks requiring alertness until response to drug is known), or headache. Report persistent abdominal pain, bloody diarrhea, and fever; symptoms of depression, suicidal ideas; unusual

bruising or bleeding, any signs or symptoms of infection, unusual fatigue, chest pain or palpitations, difficulty breathing, wheezing, severe nausea or vomiting.

REFERENCES

1Fried, MW, Shillman, ML, Reddy, KR, et al. Peginterferon Alfa-2a Plus Ribavirin for Chronic Hepatitis C Virus Infection. N Engl J Med 2002; 347:975.

2. Pegasys prescribing Information. Roche Pharmaceuticals, April 20, 2009.

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