



Peginterferon alfa-2a (Pegasys®)
Peginterferon alfa-2b (Peg-Intron®)
UTILIZATION MANAGEMENT CRITERIA

DRUG CLASS:	Pegylated Interferons
BRAND (generic) NAME:	Pegasys (peginterferon alfa-2a) Single-use vial 180 mcg/1.0 mL; Prefilled syringe 180 mcg/0.5 mL Peg-Intron (peginterferon alfa-2b) Single-use vial (with 1.25 mL diluent) and REDIPEN®: 50 mcg, 80 mcg, 120 mcg, 150 mcg per 0.5 mL.

FDA-APPROVED INDICATIONS
PEG-Intron (peginterferon alfa-2b): <u>Combination therapy with ribavirin:</u> <ul style="list-style-type: none">• Chronic Hepatitis C (CHC) in patients 3 years of age and older 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. <u>Monotherapy:</u> CHC in patients (18 years of age and older) with compensated liver disease previously untreated with interferon alpha.
Pegasys (Peginterferon alfa-2a): <ul style="list-style-type: none">• Treatment of Chronic Hepatitis C (CHC) in adults with compensated liver disease not previously treated with interferon alpha, in patients with histological evidence of cirrhosis and compensated liver disease, and in adults with CHC/HIV coinfection and CD4 count > 100 cells/mm³.<ul style="list-style-type: none">○ Combination therapy with ribavirin is recommended unless patient has contraindication to or significant intolerance to ribavirin. <u>Pegasys monotherapy is indicated for:</u> <ul style="list-style-type: none">• 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.

COVERAGE AUTHORIZATION CRITERIA

Peginterferons alfa (Pegasys and Peg-Intron) are covered for the following conditions or situations:

A. Hepatitis B

Patients with a diagnosis of chronic Hepatitis B

- Patients have no contraindications to the use of peginterferons (e.g., decompensated liver disease, autoimmune hepatitis, known hypersensitivity reactions to alpha interferons, pregnant women and men whose female partners are pregnant [when used in combination with ribavirin]).

B. Hepatitis C, Initial therapy OR Retreatment

Peginterferon is covered for the following conditions and situations:

- diagnosis of chronic Hepatitis C, AND
- baseline positive viral load (quantitative HCV-RNA) test, AND
- genotype confirmed, AND
- used in combination with ribavirin unless patient has a contraindication to or cannot tolerate ribavirin, AND
- Peginterferon is prescribed by or in consultation with a physician with expertise and experience in the management of infectious hepatitis, AND
- Patients have no contraindications to the use of peginterferons (e.g., decompensated liver disease, autoimmune hepatitis, known hypersensitivity reactions to alpha interferons, pregnant women and men whose female partners are pregnant [when used in combination with ribavirin]).

AND criteria under one of the following:

1) Peginterferon plus ribavirin used without protease inhibitor

- **Genotype 1,4,5,6 or unknown:** initial approval for 28 weeks. At 24 weeks, the viral titer must have decreased by $\geq 2 \log_{10}$ (or virus undetectable) before authorization for an additional 20 weeks of therapy (48 weeks total) will be given.
- **Genotype 2 or 3:** Approval for 24 weeks will be given. Patients who are being re-treated for HCV, those co-infected with HCV and HIV, and those using peginterferon as monotherapy: approval for 48 weeks will be given.
 - Patients with chronic hepatitis C viral genotype 3 who have a high level (as determined by the prescribing physician) of HCV RNA or advanced fibrosis may be approved for 48 weeks. (High viral load usually is considered to be $> 600,000$ or $800,000$ IU/mL.)

2) Peginterferon used in combination with TELAPREVIR (Incivek):

Initial Therapy:

- Once approval of telaprevir has been obtained, approval of peginterferon (must be used with ribavirin) will be given for 12 weeks.

Renewal Evaluation:

- For patients who are treatment-naïve and those who experienced relapse to prior interferon-based therapy:

- Undetectable HCV RNA at Treatment Week 4: approval of peginterferon (used with ribavirin) will be given for 12 more weeks after telaprevir is discontinued (total treatment duration of peginterferon 24 weeks).
- Detectable HCV RNA \leq 1,000 IU/mL at Treatment Week 4: approval of peginterferon (used with ribavirin) will be given for 36 more weeks after telaprevir is discontinued (total treatment duration of peginterferon 48 weeks).
- For patients with compensated cirrhosis/fibrosis, and null-responders and partial-responders to prior interferon-based therapy:
 - Approval of peginterferon (used with ribavirin) will be given for 36 more weeks after telaprevir is discontinued (total treatment duration of peginterferon 48 weeks).

3) Peginterferon used in combination with BOCEPREVIR (Victrelis):

- Once approval of boceprevir has been obtained for 44 weeks in the appropriate patients, approval of peginterferon (must be used with ribavirin) will be given for 48 weeks (total duration of therapy)
- Once approval of boceprevir has been obtained for patients *without* cirrhosis who experienced partial response or relapse to prior interferon-based therapy AND whose HCV RNA at 8 weeks is undetectable – Approval of peginterferon (must be used with ribavirin) will be given for 36 weeks (total duration of therapy)
- Once approval of boceprevir has been obtained for patients *without* cirrhosis who experienced partial response or relapse to prior interferon-based therapy AND whose HCV RNA at 8 weeks is detectable – Approval of peginterferon (must be used with ribavirin) will be given for 48 weeks (total duration of therapy)
- Once approval of boceprevir has been obtained for patients *without* cirrhosis who are naïve to treatment AND whose HCV RNA at 8 weeks is undetectable – Approval of peginterferon (must be used with ribavirin) will be given for 28 weeks (total duration of therapy)
- Once approval of boceprevir has been obtained for patients *without* cirrhosis who are naïve to treatment AND whose HCV RNA at 8 weeks is detectable – Approval of peginterferon (must be used with ribavirin) will be given for 48 weeks (total duration of therapy)

WARNING: RISK OF SERIOUS DISORDERS AND RIBAVIRIN-ASSOCIATED EFFECTS

- May cause or aggravate fatal or life-threatening neuropsychiatric, autoimmune, ischemic, and infectious disorders. Monitor closely and withdraw therapy with persistently severe or worsening signs or symptoms of the above disorders.

Use with Ribavirin

- Ribavirin may cause birth defects and fetal death; avoid pregnancy in female patients and female partners of male patients.
- Ribavirin is a potential carcinogen.

CONTRAINDICATIONS:

- Known hypersensitivity reactions
- Autoimmune hepatitis
- Hepatic decompensation (Child-Pugh score greater than 6 [class B and C]) in cirrhotic CHC patients before or during treatment

Additional contraindications for combination therapy with ribavirin:

- Pregnant women and men whose female partners are pregnant
- Hemoglobinopathies (e.g., thalassemia major, sickle-cell anemia)
- Creatinine clearance less than 50 mL/min

DOSAGE AND ADMINISTRATION:

- Pegasys 180 mcg/week is administered by subcutaneous injection.
- PegIntron is administered by subcutaneous injection.

	PegIntron Dose (Adults)*	PegIntron Dose (Pediatric Patients)	Ribavirin Dose* (Adults)	Ribavirin Dose (Pediatric Patients)
Peg-Intron / Ribavirin Combination Therapy	1.5 mcg/kg/ week	60 mcg/m2/ week	800-1400 mg orally daily with food	15 mg/kg/day orally with food in 2 divided doses

- The length of peginterferon treatment depends on indication, genotype, and whether it is co-administered with ribavirin and/or protease inhibitors that treat hepatitis C.
- Dose reduction is recommended in patients experiencing certain laboratory abnormalities, adverse reactions or renal dysfunction.

REFERENCES:

Pegasys (peginterferon alfa-2a) product labeling. Genentech. San Francisco, CA. 2011. <http://www.gene.com/gene/products/information/pegasys/pdf/pi.pdf>

Peg-Intron (peginterferon alfa-2b) product labeling. Schering Corporation, a subsidiary of Merck & Co., Inc. Whitehouse Station, NJ. 2011. <http://www.spfiles.com/pipeg-intron.pdf>

Incivek (telaprevir) product labeling. Vertex Pharmaceuticals Incorporated. Cambridge, MA. 2011. http://pi.vrtx.com/files/uspi_telaprevir.pdf

Victrelis (boceprevir) product labeling. Schering Corporation, a subsidiary of Merck & Co. Whitehouse Station, NJ. 2011. http://www.merck.com/product/usa/pi_circulars/v/victrelis/victrelis_pi.pdf