VENTURA COUNTY
HEALTH CARE PLAN

Prior Authorization DRUG Guidelines

PEG/INTRON®

(Pegylated interferon (peginterferon) alfa/2b)
Other Brands: PegIntron®; PegIntron™ Redipen®; Sylatron™
Effective Date: 7/28/05
Date Developed: 7/28/05 by C. Wilhelmy MD
Last Approval Date: 1/26/16, 1/24/17, 1/23/18, 1/22/19
(Archived 1/22/19)

Peg Intron 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. It 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: Peg Intron is used for the treatment of chronic hepatitis C (as monotherapy or in combination with ribavirin) in adult patients who have never received interferon alpha and have compensated liver disease. It may be prescribed for a maximum of one year.

FDA Approved Indications:

- Combination therapy with REBETOL (ribavirin): Chronic Hepatitis C (CHC) in patients greater than or equal to 3 years with compensated liver disease.
- Monotherapy: (for patients who are intolerant to ribavirin): CHC in patients with compensated liver disease previously untreated with interferon alpha and who are at least 18 years of age.

Indications and Usage Guidelines:

For all patients

- Patient is 3 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

Previously untreated patients (naive 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 (>2x 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

  - Patient has symptomatic cryoglobulinemia

    OR

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

Non-responders

- In combination with ribavirin, 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 of 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 increased to > 1000 copies/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

2. Coverage is Not Authorized For:
    - Uncontrolled autoimmune hepatitis
    - A third course of therapy for patients who have failed to achieve sustained virological response following two courses of pegylated interferon and ribavirin
    - Monotherapy with pegylated interferon, unless ribavirin is contraindicated
    - Patients with signs of liver decompensation [e.g. ascites, persistent jaundice, wasting, variceal hemorrhage, hepatic encephalopathy and preexisting cirrhosis] before or during treatment. These patients should be considered for liver transplantation. Consideration of therapy may be given to well compensated cirrhotics to avoid liver transplantation.
    - Use of PEG-Intron as prophylaxis following liver transplant even with positive Hepatitis C donor
    - Following heart, lung or kidney transplants
    - Patients with previous history of drug or alcohol abuse who have not abstained for at least 3 months before starting therapy
    - To solely reduce the risk of developing hepatocellular carcinoma (HCC) in patients with cirrhosis
    - Non-FDA approved indications, which are not listed in the Health Net Approved Indications and usage guidelines section unless there is sufficient documentation of efficacy and safety in the published literature

VCHCP requires that Peg Intron be prescribed by a gastroenterologist or a Hepatitis C Clinic physician.

MONITORING PARAMETERS — Baseline and periodic TSH, hematology (including CBC with differential, platelets), and chemistry (including LFTs) testing. Evaluate for depression and other psychiatric symptoms before and after initiation of therapy; baseline eye examination in diabetic and hypertensive patients; baseline echocardiogram in patients with cardiac disease; serum HCV RNA levels after 24 weeks of treatment

DOSING: ADULTS

Chronic hepatitis C: SubQ: Administer dose once weekly. See Lexi-Comp Online™ for details.

DOSING: PEDIATRIC — Safety and efficacy have not been established.
DOSING: ELDERLY — May require dosage reduction based upon renal dysfunction, but no established guidelines are available.
DOSING: RENAL IMPAIRMENT — Monitor for signs and symptoms of toxicity and if toxicity occurs then adjust dose. Do not use in patients with Clcr<50 mL/minute. Patients were excluded from the clinical trials if serum creatinine >1.5 times the upper limits of normal.

DOSING: HEPATIC IMPAIRMENT — Contraindicated in decompensated liver disease

ADMINISTRATION — For SubQ administration; rotate injection site

CONTRAINDICATIONS — Hypersensitivity to polyethylene glycol (PEG), interferon alfa, or any component of the formulation; autoimmune hepatitis; decompensated liver disease; previous treatment with interferon; severe psychiatric disorder; pregnancy (in combination with ribavirin)

WARNINGS / PRECAUTIONS — Severe psychiatric adverse effects, including depression, suicidal ideation, and suicide attempt, may occur; use caution with a history of depression. Avoid use in severe psychiatric disorders and discontinue if worsening or persistently severe signs/symptoms of neuropsychiatric disorders (including depression and/or suicidal thoughts/behavior) occur. Use with caution in patients who are chronically immunosuppressed, with low peripheral blood counts or myelosuppression, including concurrent use of myelosuppressive therapy. Discontinue therapy when significant decreases in neutrophil (<0.5 x 109/L) or platelet counts (<50,000/mm3 occur).

Use with caution in patients with prior cardiovascular disease, endocrine disorders, autoimmune disorders, and pulmonary dysfunction; may cause or aggravate fatal or life-threatening conditions. Discontinue therapy if colitis develops or known or suspected pancreatitis develops. Patients with renal dysfunction should be monitored for signs/symptoms of toxicity (dosage adjustment required if toxicity occurs); avoid use of combination therapy with ribavirin in renal dysfunction (Clcr<50 mL/minute). Ophthalmologic disorders (including retinal hemorrhages, cotton wool spots, and retinal artery or vein obstruction) have occurred in patients using other alpha interferons. Prior to start of therapy, visual exams are recommended for patients with diabetes mellitus or hypertension. Transient rashes do not necessitate interruption of therapy.

Due to differences in dosages, patients should not change brands. Safety and efficacy have not been established in patients who have failed other alpha interferon (including

peginterferon alfa-2b) therapy, received organ transplants, been infected with HIV or hepatitis B, or received treatment for >48 weeks. Use caution in geriatric patients. Safety and efficacy have not been established in children.

DRUG INTERACTIONS — Inhibits CYP1A2 (weak)
ACE inhibitors: Interferons may increase the risk of neutropenia. Risk: Monitor
Clozapine: A case report of agranulocytosis with concurrent use.
Erythropoietin: Case reports of decreased hematopoietic effect
Fluorouracil: Concentrations of fluorouracil doubled in patients with gastrointestinal carcinoma who received interferon alpha-2b.
Melphalan: Interferon alpha may decrease the serum concentrations of melphalan. Risk: Monitor.
Prednisone: Prednisone may decrease the therapeutic effects of interferon alpha. Risk: Moderate.
Theophylline: Interferon alpha may decrease the P450 isoenzyme metabolism of theophylline. Risk: Moderate.
Warfarin: Interferons may increase the anticoagulant effects of warfarin. Risk: Monitor.
Zidovudine: Interferons may decrease the metabolism of zidovudine. Risk: Monitor

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

PREGNANCY RISK FACTOR — C as monotherapy; X in combination with ribavirin

PREGNANCY IMPLICATIONS — Very high doses are abortifacient in Rhesus monkeys. Assumed to have abortifacient potential in humans. Case reports of use in pregnant women (usually interferon alfa-2a) did not result in adverse effects in the fetus or newborn. There are no adequate and well-controlled studies in pregnant women. Risk of maternal-infant transmission of hepatitis C is <5%. Reliable contraception should be used in women of childbearing potential. Not recommended for use in pregnancy (per manufacturer).

LACTATION — Excretion in breast milk unknown/not recommended

BREAST-FEEDING CONSIDERATIONS — Case report of interferon alfa-2b: Too large in molecular weight to transfer into human milk in clinically relevant amounts. Breast-feeding is not linked to the spread of hepatitis C virus; however, if nipples are cracked or bleeding, breast-feeding is not recommended.

PATIENT EDUCATION — Blood work will be done before the start of this medicine and during its use. Maintain adequate hydration (2-3 L/day of fluids unless instructed to restrict fluid intake). 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
1. Heathcote, EJ, Shiffman, ML, Cooksley, GE, et al. Peginterferon Alfa-2a in Patients With Chronic Hepatitis C and Cirrhosis. N Engl J Med 2000; 343:1673.
2. Kumar, AR, Hale, TW, Moke, RE. Transfer of Interferon Alfa Into Human Breast Milk. J Hum Lact 2000; 16:226.
3. Zeuzem, S, Feinman, SV, Rasenack, J, et al. Peginterferon Alfa-2a in Patients With Chronic Hepatitis C. N Engl J Med 2000; 343:1666.
4. PEGIntron Prescribing information, Schering Corporation. May 08, 2009

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