# Hepatitis B/Hepatitis C Peg-interferon Prior Authorization Program Summary

This program applies to Commercial, GenPlus, NetResults A series, SourceRx and Health Insurance Marketplace formularies.

**OBJECTIVE**
The intent of the Peginterferon Prior Authorization (PA) program is to appropriately select patients for therapy according to the Food and Drug Administration (FDA) approved product labeling and/or clinical guidelines and/or clinical studies. The PA process will evaluate the use of these agents when there is supporting clinical evidence for their use.

**TARGET DRUGS**
**Pegasys®** (peginterferon alfa-2a)
**Pegintron®** (peginterferon alfa-2b)

| Brand (generic) | GPI | Multisource Code |
|---|---|---|
| **Pegasys (peginterferon alfa-2a)** | | |
| 180 mcg/0.5 ml injection | 12353060052040 | M, N, O, or Y |
| 180 mcg/ml injection (vial) | 12353060052020 | M, N, O, or Y |
| **Pegasys Proclick (peginterferon alfa-2a)** | | |
| 135 mcg/0.5 mL injection | 12353060052030 | M, N, O, or Y |
| 180 mcg/0.5 mL injection | 12353060052040 | 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 |

**PRIOR AUTHORIZATION CRITERIA FOR APPROVAL**
**Pegasys or PegIntron** will be approved when ALL of the following criteria are met:

1. The patient does not have any FDA labeled contraindications to the requested agent
   **AND**
2. ONE of the following:
   a. The patient has no known history of illicit drug and/or alcohol abuse and/or high risk sexual practices
      **OR**
   b. The patient has a history of illicit drug and/or alcohol abuse and/or high risk sexual practices and ONE of the following:
      i. The patient has abstained from the use of illicit drugs, alcohol abuse, and/or high risk sexual practices for the past 12 months or for a length of time at the discretion of the provider to determine readiness for treatment
         **OR**
      ii. The patient is actively participating in a recovery program and will not continue to actively abuse illicit drugs, abuse alcohol, or participate in high risk sexual practices

   **AND**
3. ONE of the following:
   a. Therapy is not being requested for treatment of a patient re-infected with hepatitis C
      **OR**

b. Therapy is being requested for a patient re-infected with hepatitis C following liver transplantation

**AND**

4. ONE of the following:
   a. The patient has a diagnosis of chronic hepatitis B and BOTH of the following:
      i. The chronic hepatitis B infection has been confirmed by serological markers **AND**
      ii. The patient has not been administered peg-interferon for more than 18 months for treatment of chronic hepatitis B

      **OR**

   b. BOTH of the following:
      i. The patient has a diagnosis of chronic hepatitis C genotype 1, 2, 3, or 4 **AND**
      ii. The requested agent will be used in a treatment regimen AND length of therapy recommended for the patient's genotype as noted in Table 1, 2, 3, and 4 (FDA labeling)

**Length of approval: Hepatitis B:** Up to 18 months
**Hepatitis C:** Up to the duration as determined in Table 1, 2, 3, and 4

**Table 1: Olysio, Peg-interferon (PEG-IFN), and Ribavirin Treatment Recommendations based on FDA labeling**

| Genotype | Patient population | Treatment regimen | Duration of therapy |
|---|---|---|---|
| 1 or 4 | Treatment naïve and prior relapsers* HCV monoinfected patients without cirrhosis or with compensated cirrhosis (Child-Pugh A) | Olysio + PEG-IFN + RBV | Olysio: 12 weeks<br>PEG-IFN: 24 weeks |
| | Treatment naïve and prior relapsers* with HCV/HIV co-infected patients without cirrhosis | Olysio + PEG-IFN + RBV | Olysio:12 weeks<br>PEG-IFN: 24 weeks |
| | Treatment naïve and prior relapsers* with HCV/HIV co-infection with compensated cirrhosis (Child-Pugh A) | Olysio + PEG-IFN + RBV | Olysio: 12 weeks<br>PEG-IFN: 48 weeks |
| | Prior non-responders (including partial± and null responders^) without cirrhosis or with compensated cirrhosis (Child-Pugh A) and with or without HIV co-infection | Olysio + PEG-IFN + RBV | Olysio: 12 weeks<br>PEG-IFN: 48 weeks |

*Prior relapse: HCV RNA not detected at the end of prior IFN based therapy and HCV RNA detected during follow up.
± Prior partial responder: Prior on-treatment ≥ 2 log10 IU/mL reduction in HCV RNA from baseline at week 12 and HCV RNA detected at the end of prior IFN based therapy.
^ Prior null responder: Prior on treatment < 2 log 10 reduction in HCV RNA from baseline at week 12 during prior IFN based therapy.

**Table 2: Sovaldi + PEG-IFN + RBV Treatment Recommendations based on FDA approved labeling**

| Genotype* | FDA approved regimen | Duration of therapy |
|---|---|---|
| 1a or 1b | Sofosbuvir + PEG-IFN + RBV | 12 weeks |
| 4 | Sofosbuvir + PEG-IFN + RBV | 12 weeks |

*Includes patients with HCV/HIV co-infection

**Table 3: Pegasys + RBV Treatment Recommendations based on FDA labeling**

| Genotype | FDA approved regimen | Duration of therapy |
|---|---|---|
| 1 or 4 | Pegasys + RBV | 48 weeks |
| 2 or 3 | Pegasys + RBV | 24 weeks |
| 5 or 6 | There is insufficient data for dosage | |

| | | |
|---|---|---|
| | and duration | |

**Table 4: PegIntron + RBV Treatment Recommendations based on FDA labeling**

| Genotype | FDA approved regimen | Duration of therapy |
|---|---|---|
| 1 | PegIntron + RBV | 48 weeks |
| 2 or 3 | PegIntron + RBV | 24 weeks |

**Contraindications:**

| Agent(s) | Contraindication(s) |
|---|---|
| **Pegasys** (peginterferon alfa-2a) | Known hypersensitivity reactions such as urticaria, angioedema, bronchoconstriction, anaphylaxis, or Stevens-Johnson syndrome to alpha interferons, including Pegasys, or any of its components.<br>Autoimmune hepatitis.<br>Hepatic decompensation (Child-Pugh score greater than 6 [class B and C]) in cirrhotic patients before treatment.<br>Hepatic decompensation with Child-Pugh score greater than or equal to 6 in cirrhotic CHC patients coinfected with HIV before treatment.<br>In neonates and infants because it contains benzyl alcohol.<br>When used in combination with other HCV antiviral drugs, the contraindications applicable to those agents are applicable to combination therapies.<br>Pegasys combination treatment with ribavirin is contraindicated in women who are pregnant and men whose female partners are pregnant. |
| **PegIntron** (peginterferon alfa-2b) | Known hypersensitivity reactions, such as urticaria, angioedema, bronchoconstriction, anaphylaxis, Stevens-Johnson syndrome, and toxic epidermal necrolysis to interferon alpha or any other component of the product.<br>Autoimmune hepatitis.<br>Hepatic decompensation (Child-Pugh score greater than 6 [class B and C]) in cirrhotic CHC patients before or during treatment.<br>PegIntron/ribavirin combination therapy is additionally contraindicated in women who are pregnant. Ribavirin may cause fetal harm when administered to a pregnant woman. Ribavirin is contraindicated in women who are or may become pregnant. If ribavirin is used during pregnancy, or if the patient becomes pregnant while taking ribavirin, the patient should be apprised of the potential hazard to her fetus.<br>Men whose female partners are pregnant.<br>Patients with hemoglobinopathies (e.g., thalassemia major, sickle-cell anemia).<br>Patients with creatinine clearance less than 50 mL/min. |

*pharmacy literature; and/or (iii) review of common medical practices in the treatment and diagnosis of disease as of the date hereof. Physicians and other providers are solely responsible for all aspects of medical care and treatment, including the type, quality, and levels of care and treatment.*

*The purpose of Blue Cross and Blue Shield of Alabama's pharmacy policies are to provide a guide to coverage. Pharmacy policies are not intended to dictate to physicians how to practice medicine. Physicians should exercise their medical judgment in providing the care they feel is most appropriate for their patients.*

*Neither this policy, nor the successful adjudication of a pharmacy claim, is guarantee of payment.*

**FDA APPROVED INDICATIONS AND DOSAGE** [1,2]

| Agents* | Indications | Dose and Interval¥ |
|---|---|---|
| **Pegasys** (peginterferon alfa-2a) | Hepatitis C, in combination with other hepatitis C virus (HCV) antiviral drugs in patients 5 years of age and older with compensated liver disease | **Genotype 1- 4:** 180 mcg subcutaneous once weekly **Genotype 5, 6:** There is insufficient data for dosage recommendations |
| | Hepatitis C, as monotherapy, only in patients with contraindication or significant intolerance to other HCV antiviral drugs | |
| | HBeAg positive and HBeAG negative Hepatitis B in adult patients with compensated liver disease and evidence of viral replication and liver inflammation | 180 mcg subcutaneous once weekly |
| **Pegintron** (peginterferon alfa-2b) | Chronic Hepatitis C with compensated liver disease | **Adult dose:** 1.5 mcg/kg/week |
| | | **Pediatric dose:** 60 mcg/$m^{2/}$week |

* For peg-interferons for oncology (e.g. Sylatron) and Multiple sclerosis (e.g. Plegridy), refer to the SA Oncology PA/QL and Multiple Sclerosis PA/QL programs respectively.
¥ Duration of treatment is dependent upon the genotype and the regimen in which the peg-interferon is used

**Hepatitis B Disease Background**[5]
Hepatitis B is an infection of the liver caused by the Hepatitis B virus (HBV). The prevalence of chronic HBV infection is estimated at 240 million persons globally and 704,000 persons in the United States. Deaths due to cirrhosis and cancer secondary to chronic HBV infection are estimated at 310,000 and 340,000 per year respectively. The goal of treatment of chronic HBV infection is to decrease morbidity and mortality.
Diagnosis of Hepatitis B infection should include lab tests to confirm HBV serology and HBV replication. A thorough clinical history and physical examination should also be performed. Checking for other viral infections such as hepatitis C and HIV are also recommended.

**Initial Evaluation of HBaAG-Positive* Patients**

| | History/Physical Examination | Routine Laboratory Tests | Serology/Virology | Imaging/Staging Studies |
|---|---|---|---|---|
| All patients | Symptoms/signs of cirrhosis<br>Alcohol and metabolic risk factors<br>Family history of HCC<br>Vaccination status | CBC including platelet count, AST, ALT, total bilirubin, alkaline phosphatase, albumin, INR | HBeAg/anti-HBe<br>HBV DNA quantitation<br>Anti-HAV to determine need for vaccination | Abdominal ultrasound<br>Vibration-controlled transient elastography or serum fibrosis panel (APRI, FIB-4, or FibroTest) |
| Select patients | | Tests to rule out other causes of chronic liver diseases if elevated liver test(s)<br>AFP, GGT | HBV genotype<br>Anti-HDV<br>Anti-HCV<br>Anti-HIV in those who have not undergone one-time screening (ages 13-64) | Liver biopsy |

Abbreviation:s INR, international normalized ratio; GGT, gamma-glutamyl transpeptidase.

*HBaSG-Hepatitis B surface antigen

There are several agents currently indicated for treatment of chronic HBV. They include Peg-interferon, lamivudine, telbivudine, entecavir, tenofovir and adefovir. AASLD recommends peg-interferon, entecavir, or tenofovir as preferred initial therapy for adults with immune-active chronic HBV infection.

Peginterferon alfa-2a has an FDA approved indication for chronic hepatitis B while peginterferon alfa-2b is not FDA approved for chronic hepatitis B; however, there are studies that support its use for this indication.

**Hepatitis C Disease Background** [3,4]
Hepatitis C is an infection of the liver caused by the Hepatitis C virus (HCV) and is one of the leading causes of chronic liver disease in the United States. According to the Centers for Disease Control and Prevention

(CDC), there were an estimated 3.5 million people infected with hepatitis C as of 2015. Hepatitis C infection can either be acute or chronic. Acute HCV infection is defined as presenting within 6 months following exposure to the virus. The infection is defined as chronic if the virus is present beyond 6 months following exposure. 70% to 80% of those infected with HCV will go on to develop chronic HCV infection.
The goal of hepatitis C therapy is to eradicate the virus and prevent liver damage including cirrhosis. The American Association of the Study of Liver Disease (AASLD) and the Infectious Disease Society of America (IDSA) have developed guidelines to aid in the management of hepatitis C. The guidelines address issues ranging from testing and linkage to care to the optimal treatment regimen based on patient situations.

AASLD/IDSA guidelines recommend direct acting antivirals (DAAs) as the mainstay of treatment for chronic HCV infection. Certain DAAs may be used as monotherapy while others require use in combination with other agents including peg-interferon, ribavirin, and other DAAs. The AASLD/IDSA treatment guidelines recommend against treatment of chronic hepatitis C with peg-interferon based regimens as they are considered inferior to the non-peg-interferon DAA based regimens.

**AASLD/IDSA guidelines on when and in whom to treat**[4]
The goal of therapy is to reduce all-cause mortality and liver-related health adverse consequences, including end-stage liver disease and hepatocellular carcinoma, by the achievement of virologic. According to the AASLD/IDSA guidelines, treatment is recommended for all patients with chronic HCV infection, except those with short life expectancies that cannot be remediated by treating HCV, by transplantation, or by other directed therapy. Treatment should be initiated early because delaying therapy may decrease the benefits of eradicating the hepatitis C viral infection.

**References**


1. Pegasys prescribing information. July 2015.
2. PegIntron prescribing information. February 2016.
3. AASLD/IDSA HCV Guidance: Recommendations for Testing, Managing, and Testing Hepatitis C. Available at www.hcvguidelines.org. Accessed May 2017.
4. The center for Disease Control and Prevention. Viral Hepatitis Statistics and Surveillance. Available at http://www.cdc.gov/hepatitis/statistics. Accessed June 2016.
5. AASLD Guidelines for Treatment of Chronic Hepatitis B. https://www.aasld.org/sites/default/files/guideline_documents/hep28156.pdf. Accessed May 2017.