Peg-interferon Prior Authorization Program Summary

Your health benefit plan may not cover certain prescription drug products or drug categories included in this document. Please consult your benefit plan materials for details about your particular benefit.

This document may include drugs that are not included on your plan's formulary. For drug coverage status, please consult your plan's formulary.

FDA APPROVED INDICATIONS AND DOSAGE [1,2]

Agent(s)*	Indication(s)	Dosage
Pegasys® (peginterferon alfa-2a) Injection for subcutaneous use	• **Chronic hepatitis C:** - Adult patients with compensated liver disease: ▪ In combination with other hepatitis C virus (HCV) antiviral drugs ▪ As monotherapy only in patients with contraindication or significant intolerance to other HCV antiviral drugs - Pediatric patients 5 years of age and older with compensated liver disease in combination with ribavirin Limitations of Use: Pegasys alone or in combination with ribavirin without additional HCV antiviral drugs is not recommended for treatment of patients with chronic hepatitis c who previously failed therapy with an interferon-alfa Pegasys is not recommended for treatment of patients with chronic hepatitis C who have had solid organ transplantation • **Chronic hepatitis B:** - Adult patients: ▪ Treatment of HBeAG positive and HBeAG negative patients with compensated liver disease and evidence of viral replication and liver inflammation - Pediatric patients:	**Chronic hepatitis C:** Adult patients: Genotype 1- 4: 180 mcg subcutaneous once weekly Genotype 5, 6: There is insufficient data for dosage recommendations Pediatric patients: 180 mcg/1.73 m^2 X BSA subcutaneously, to a maximum dose of 180 mcg, once weekly Duration of treatment for hepatitis C is dependent on the genotype and concomitant medications used **Chronic hepatitis B:** Adult patients: 180 mcg subcutaneously once weekly for 48 weeks

	▪ Treatment of non-cirrhotic, HBeAG-positive patients 3 years of age and older with evidence of viral replication and elevations in serum alanine aminotransferase (ALT)	Pediatric patients: 180 mcg/1.73 m^2 X BSA, up to a maximum of 180 mcg, subcutaneously once weekly for 48 weeks
PegIntron® (peginterferon alfa-2b) Injection for subcutaneous use	• 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.

Clinical Rational
Hepatitis B[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.

The presence of hepatitis B surface antigen (HB_sAg) establishes the diagnosis of hepatitis B. Chronic infection is defined by the presence of HB_sAg for at least 6 months. HBV is transmitted by perinatal, percutaneous, and sexual exposure and by close person-to-person contact (presumably by open cuts and sores, especially among children in hyper pandemic areas). HB_sAg and antibody to hepatitis B surface antigen (anti-HB_s) should be used for screening and indication for immunization. Alternatively, antibody to hepatitis B core antigen (anti-HB_c) can be utilized for screening as long as those who test positive are further tested for both HB_sAg and anti-HB_s to differentiate current infection from previous infection. HBC vaccination does not lead to anti-HB_c positivity.

Interpretation of Screening Tests for HBV Infection

Screening Test Results					
HB_sAg	Anti-HB_c	Anti- HB_s	Interpretation	Management	Vaccinate
+	+	-	Chronic hepatitis B	Additional testing and management needed	No
-	+	+	Past HBV infection, resolved	No further management unless immunocompromised or undergoing chemotherapy or immunosuppressive therapy	No
-	+	-	Past HBV infection, resolved or false-positive	HBV DNA testing if immunocompromised patient	Yes, if not from area of intermediate or high endemicity

-	-	+	Immune	No further testing	No
-	-	-	Uninfected and not immune	No further testing	Yes

There are several agents currently indicated for treatment of chronic HBV. They include adefovir, entecavir, lamivudine, peg-interferon-α-2a, peg-interferon-α-2b, telbivudine, tenofovir alafenamide, and tenofovir dipovoxil fumarate. AASLD prefers entecavir, peg-interferon-α-2a (in adults), peg-interferon-α-2b (in children), tenofovir alafenamide, and tenofovir dipovoxil fumarate as initial therapy for adults 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[3,4]
Hepatitis C is an infection of the liver caused by the Hepatitis C virus (HCV), a blood-borne virus. Today, most people become infected with HCV by sharing needles or other equipment to inject drugs. Hepatitis C infection can either be acute or chronic. Acute HCV infection is defined as presenting within 6 months following exposure to the virus. In 2018, the reported acute hepatitis C case count in the United States corresponded to a rate of 1.2 cases per 100,000 population, an over 71% increase from the reported incidence rate in 2014. The infection is defined as chronic if the virus is present beyond 6 months following exposure. More than 50% of people who become infected with HCV develop chronic infection. Chronic hepatitis C is a serious disease that can result in cirrhosis, liver cancer, and death [4]

The American Association for the Study of Liver diseases (AASLD) along with the Infectious Diseases society of America (IDSA) recommend the following:[9]
- One-time, routine, opt out HCV testing is recommended for all individuals aged 18 years and older
- One-time HCV testing should be performed for all persons less than 18 years old with activities, exposures, or conditions or circumstances associated with an increased risk of HCV infection
- Prenatal HCV testing as part of routine prenatal care is recommended with each pregnancy
- Periodic repeat HCV testing should be offered to all persons with activities, exposures, or conditions or circumstances associated with an increased risk of HCV exposure
- Annual HCV testing is recommended for all persons who inject drugs, for HIV-infected men who have unprotected sex with men, and men who have sex with men taking pre-exposure prophylaxis (PrEP)

Risk activities:
- Injection drug use (current or ever, including those who injected only once)
- Intranasal illicit drug use
- Men who have sex with men

Risk exposures:
- Persons on long-term hemodialysis (ever)
- Persons with percutaneous/parenteral exposures in an unregulated setting
- Healthcare, emergency medical, and public safety workers after needlestick, sharps, or mucosal exposure to HCV-infected blood
- Children born to HCV-infected women
- Prior recipients of a transfusion or organ transplant, including persons who:
    - Were notified that they received blood from a donor who later tested positive for HCV
    - Received a transfusion of blood or blood components, or underwent an organ transplant before July 1992
    - Received clotting factor concentrates produced before 1987
- Persons who were ever incarcerated

Other conditions and circumstances:
- HIV infection

- Sexually active persons about to start pre-exposure prophylaxis (PrEP) for HIV
- Chronic liver disease and/or chronic hepatitis, including unexplained elevated alanine aminotransferase (ALT) levels
- Solid organ donors (living and deceased) and solid organ transplant recipients

AASLD/IDSA guidelines on when and in whom to initiate HCV therapy
The goal of treatment of HCV-infected persons 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 cure as evidenced by a sustained virologic response (SVR) (defined as the continued absence of detectable HCV RNA for at least 12 weeks after completion of therapy). According to the AASLD/IDSA guidelines, treatment is recommended for all patients with acute or 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 SVR and increase the rates of liver-related mortality.[3]

Safety[1-2]
Pegasys and PegIntron both contain boxed warnings about fatal or life-threatening neuropsychiatric, autoimmune, ischemic, and infectious disorders.

PegIntron also contains a boxed warning about avoiding pregnancy if the agent is used with ribavirin.

Pegasys (peginterferon alfa-2a) is contraindicated in:
- Known hypersensitivity reactions such as urticaria, angioedema, bronchoconstriction, anaphylaxis, or Stevens-Johnson syndrome to alpha interferons, including Pegasys, or any of its components
- Autoimmune hepatitis
- Hepatic decompensation (Child-Turcotte-Pugh score greater than 6 [class B and C]) in cirrhotic patients before treatment
- Hepatic decompensation with Child-Turcotte-Pugh score greater than or equal to 6 in cirrhotic CHC patients coinfected with HIV before treatment
- In neonates and infants because it contains benzyl alcohol
- When used in combination with other HCV antiviral drugs, the contraindications applicable to those agents are applicable to combination therapies
- Pegasys combination treatment with ribavirin is contraindicated in women who are pregnant and men whose female partners are pregnant

PegIntron (peginterferon alfa-2b) is contraindicated in:
- 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
- Autoimmune hepatitis
- Hepatic decompensation (Child-Turcotte-Pugh score greater than 6 [class B and C]) in cirrhotic CHC patients before or during treatment
- If PegIntron is administered with ribavirin, the contraindicated to ribavirin also apply to this combination regimen

References

1. Pegasys prescribing information. March 2021.
2. PegIntron prescribing information. January 2019.
3. AASLD/IDSA HCV Guidance: Recommendations for Testing, Managing, and Testing Hepatitis C. Available at www.hcvguidelines.org.
4. The center for Disease Control and Prevention. Viral Hepatitis Statistics and Surveillance. Available at http://www.cdc.gov/hepatitis/statistics.
5. AASLD Guidelines for Treatment of Chronic Hepatitis B. https://www.aasld.org/sites/default/files/HBVGuidance_Terrault_et_al-2018-Hepatology.pdf.

Peginterferon Prior Authorization

TARGET AGENT(S)
Pegasys® (peginterferon alfa-2a)
PegIntron® (peginterferon alfa-2b)

Brand (generic)	GPI	Multisource Code
Pegasys (peginterferon alfa-2a)		
180 mcg/0.5 ml injection	1235306005E540	M, N, O, or Y
180 mcg/ml injection (vial)	12353060052020	M, N, O, or Y
Pegasys Proclick (peginterferon alfa-2a)		
180 mcg/0.5 mL injection	1235306005D540	M, N, O, or Y
PegIntron (peginterferon alfa-2b)		
50 mcg/0.5 ml injection	12353060106410	M, N, O, or Y

PRIOR AUTHORIZATION CRITERIA FOR APPROVAL
Target Agent(s) will be approved when ALL of the following are met:

1. 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 48 weeks for treatment of chronic hepatitis B
   OR
   B. The patient has a diagnosis of chronic hepatitis C genotype 1, 2, 3, or 4 AND 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)
   AND
2. ONE of the following:
   A. The patient's age is within FDA labeling for the requested indication for the requested agent
   OR
   B. The prescriber has provided information in support of using the requested agent for the patient's age
   AND
3. The patient does NOT have any FDA labeled contraindications to the requested agent

Length of approval: Hepatitis B: Up to 48 weeks total length of treatment
Hepatitis C: Up to the duration as determined in Table 1, 2, or 3

Table 1: 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 2: 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 3: 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