Peginterferon Prior Authorization Program Summary

POLICY REVIEW CYCLE

Effective Date 10-01-2024

Date of Origin

FDA LABELED INDICATIONS AND DOSAGE

Agent(s)	FDA Indication(s)	Notes	Ref#
Pegasys®* (peginterferon alfa-2a) Injection for subcutaneous use	**Chronic hepatitis C:** • Adult patients: In combination with other hepatitis C virus (HCV) drugs for adults with compensated liver disease. Pegasys monotherapy is indicated only if patient has contraindication or significant intolerance to other HCV drugs • Pediatric patients: In combination with ribavirin for pediatric patients 5 years of age and older with compensated liver disease 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 adults with HBeAg positive and HBeAg negative chronic hepatitis B (CHB) infection who have compensated liver disease and evidence of viral replication and liver inflammation Pediatric patients: Treatment of non-cirrhotic, HBeAg-positive patients 3 years of age and older with HBeAg positive CHB and evidence of viral replication and elevations in serum alanine aminotransferase (ALT)	* For peg-interferons for Multiple sclerosis (e.g. Plegridy), refer to the Multiple Sclerosis PA/QL program	1

See package insert for FDA prescribing information: https://dailymed.nlm.nih.gov/dailymed/index.cfm

CLINICAL RATIONALE

Hepatitis B	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.(5) The presence of hepatitis B surface antigen (HBsAg) establishes the diagnosis of hepatitis B. Chronic infection is defined by the presence of HBsAg 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). HBsAg and antibody to hepatitis B surface antigen (anti-HBs) should be used for screening and indication for immunization. Alternatively, antibody to hepatitis B core antigen (anti-HBc) can be utilized for screening as long as those who test positive are further tested for both HBsAg and anti-HBs to differentiate current infection from previous infection. HBC vaccination does not lead to anti-HBc positivity.(5) 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.(5)
Hepatitis C	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.(3,4) 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 ○ Use of glass crack pipes ○ Male engagement in sex with men ○ Engagement in chem sex (defined as the intentional combining of sex with the use of particular nonprescription [illicit] drugs in order to facilitate or enhance the sexual encounter) • 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 ○ Recipients of a prior 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 o Persons who were ever incarcerated • Other conditions and circumstances: o HIV infection or HBV infection o Sexually active persons about to start pre-exposure prophylaxis (PrEP) for HIV o Chronic liver disease and/or chronic hepatitis, including unexplained elevated alanine aminotransferase (ALT) levels o Solid organ donors (living and deceased) and solid organ transplant recipients
AASLD/IDSA guidelines on when and in whom to treat	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)
National Comprehensive Cancer Network supported indications	The National Comprehensive Cancer Network (NCCN) lists peginterferon as Category 2A treatment in the following indications (treatment lengths are from the studies NCCN used to support this level of evidence): • Chronic myeloid leukemia(6) o Therapy should be continued until progression to accelerated phase, blast crisis or death, or the development of intolerance to treatment whichever occurs first(7) • Hairy cell leukemia(8) o Therapy should be continued long-term (up to 164 months studied)(9) o Erdheim-Chester disease (ECD)(10) o The optimal duration of treatment is unclear but long-term (up to 3 years) treatment with peginterferon alfa (180 mcg/week) was found to have greater efficacy in high-risk ECD with stabilization or improvement in 64% of CNS disease and 79% cardiac disease(11) • Myelofibrosis(12) o In a phase III study, the mean time on peginterferon- alfa 2a therapy was 20.6 months (range 6-56)(13) o Polycythemia Vera(12) o In a phase II trial, patients were taken off study if they had not reached complete response after 6 months or at any time if they did not tolerate side effects(14) o Essential thrombocythemia(12) o In a phase II trial, patients were taken off study if they had not reached complete response after 6 months or at any time if they did not tolerate side effects(14) • Primary cutaneous CD30+ T-cell lymphoproliferative disorders(15) o Tumor regression should be experienced within 20 weeks(16) • Mycosis fungoides/Sezary Syndrome(15) o Real world data suggests complete response should be reached within 12 weeks(17) • Systemic mastocytosis(18) o Time to best response may be a year or longer(19) • Adult T-Cell leukemia/lymphoma(20)

	○ Treatment was continued for at least four weeks after the onset of complete remission or for up to one year in the absence of such a remission(21)
Safety	Pegasys contains a boxed warning about fatal or life-threatening neuropsychiatric, autoimmune, ischemic, and infectious disorders.(1) Pegasys (peginterferon alfa-2a) is contraindicated in:(1) • 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

REFERENCES

Number	Reference
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2	Reference no longer used.
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 https://www.cdc.gov/hepatitis/statistics/index.htm.
5	AASLD Guidelines for Treatment of Chronic Hepatitis B. https://www.aasld.org/practice-guidelines.
6	National Comprehensive Cancer Network (NCCN). NCCN Guidelines Chronic Myeloid Leukemia. Version 2.2024.
7	Hochhaus A, Larson RA, Guilhot F, et al. Long-Term Outcomes of Imatinib Treatment for Chronic Myeloid Leukemia. *N Engl J Med*. 2017;376(10):917-927. doi:10.1056/NEJMoa1609324
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9	Bohn JP, Gastl G, Steurer M. Long-term treatment of hairy cell leukemia with interferon-α: still a viable therapeutic option. Memo. 2016;9:63-65. doi: 10.1007/s12254-016-0269-1. Epub 2016 Jun 17. PMID: 27429657; PMCID: PMC4923076.
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12	National Comprehensive Cancer Network (NCCN). NCCN Guidelines Myeloproliferative Neoplasms. Version 1.2024.
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Number	Reference
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14	Samuelsson J, Hasselbalch H, Bruserud O, Temerinac S, Brandberg Y, Merup M, Linder O, Bjorkholm M, Pahl HL, Birgegard G; Nordic Study Group for Myeloproliferative Disorders. A phase II trial of pegylated interferon alpha-2b therapy for polycythemia vera and essential thrombocythemia: feasibility, clinical and biologic effects, and impact on quality of life. Cancer. 2006 Jun 1;106(11):2397-405. doi: 10.1002/cncr.21900. PMID: 16639737.
15	National Comprehensive Cancer Network (NCCN), NCCN Guidelines Primary Cutaneous Lymphomas. Version 1.2024.
16	Antonio Cozzio, Werner Kempf, Regula Schmid-Meyer, Michel Gilliet, Sonja Michaelis, Leo Schärer, Günter Burg & Reinhard Dummer (2006) Intra-lesional low-dose interferon α2a therapy for primary cutaneous marginal zone B-cell lymphoma, Leukemia & Lymphoma, 47:5, 865-869, DOI: 10.1080/10428190500399698.
17	Zhang SY, Liu ZR, Yang L, Wang T, Liu J, Liu YH, Fang K. Real-world data on the effectiveness and safety of interferon-alpha-2a intralesional injection for the treatment of focally recalcitrant mycosis fungoides. Ann Transl Med. 2020 Aug;8(15):920. doi: 10.21037/atm-20-1458. PMID: 32953720; PMCID: PMC7475424.
18	National Comprehensive Cancer Network (NCCN). NCCN Guidelines Systemic Mastocytosis. Version 2.2024.
19	Pardanani A. Systemic mastocytosis in adults: 2019 update on diagnosis, risk stratification and management. Am J Hematol. 2019 Mar;94(3):363-377. doi: 10.1002/ajh.25371. Epub 2019 Jan 2. PMID: 30536695.
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POLICY AGENT SUMMARY PRIOR AUTHORIZATION

Target Brand Agent(s)	Target Generic Agent(s)	Strength	Targeted MSC	Available MSC	Final Age Limit	Preferred Status
Pegasys	peginterferon alfa-	180 MCG/0.5ML ; 180 MCG/ML	M ; N ; O ; Y	N		

CLIENT SUMMARY – PRIOR AUTHORIZATION

Target Brand Agent Name(s)	Target Generic Agent Name(s)	Strength	Client Formulary
Pegasys	peginterferon alfa-	180 MCG/0.5ML ; 180 MCG/ML	Accord Enhanced ; Accord Standard ; Choice Net R – F Performance ; Choice NetR – A Select ; Choice NetR-HIM

PRIOR AUTHORIZATION CLINICAL CRITERIA FOR APPROVAL

Module	Clinical Criteria for Approval
	Initial Evaluation

Module	Clinical 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:
      1. The chronic hepatitis B infection has been confirmed by serological markers **AND**
      2. The patient has not been administered peg-interferon for 48 weeks or longer 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, or 3 (FDA labeling) **OR**
   C. The patient has a diagnosis of polycythemia vera **OR**
   D. The patient has a diagnosis of essential thrombocythemia **OR**
   E. The patient has a diagnosis of mycosis fungoides/Sezary syndrome **OR**
   F. The patient has another FDA labeled indication for the requested agent and route of administration **OR**
   G. The patient has another indication that is supported in compendia for the requested agent and route of administration **AND**
2. If the patient has an FDA labeled indication, then ONE of the following:
   A. The patient's age is within FDA labeling for the requested indication for the requested agent **OR**
   B. There is support for using the requested agent for the patient's age for the requested indication **AND**
3. The requested quantity (dose) does not exceed the maximum FDA labeled or compendia supported dose for the requested indication **AND**
4. The patient does NOT have any FDA labeled contraindications to the requested agent

Compendia Allowed: NCCN 1 or 2a recommended use

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
- **Polycythemia vera or essential thrombocythemia:** 6 months
- **Mycosis fungoides/Sezary syndrome:** 12 weeks
- **All other indications:** 12 months or for duration supported in FDA label or compendia whichever is shorter

Table 1: Sovaldi + PEG + RBV Treatment Recommendations based on FDA labeling

Genotype*	FDA labeled regimen	Duration of therapy
1a or 1 b	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 labeled 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	

Module	Clinical Criteria for Approval
	Renewal Evaluation **Target Agent(s)** will be approved when ALL of the following are met: 1. The patient has been previously approved for the requested agent through the plan's Prior Authorization process [Note: patients not previously approved for the requested agent will require initial evaluation review] **AND** 2. ONE of the following: A. The patient has a diagnosis of chronic hepatitis B AND the patient has NOT been administered peg-interferon for 48 weeks or longer 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 patient did not complete the duration of therapy for the treatment regimen recommended for the patient's genotype as noted in tables 1, 2, or 3 **OR** C. The patient has another diagnosis AND has shown clinical benefit with the requested agent **AND** 3. The requested quantity (dose) does not exceed the maximum FDA labeled or compendia supported dose for the requested indication **AND** 4. The patient does NOT have any FDA labeled contraindications to the requested agent **Compendia Allowed:** NCCN 1 or 2a recommended use **Length of approval:** • **Hepatitis B:** Up to duration to complete 48 weeks total length of treatment • **Hepatitis C:** Up to the duration to complete the regimen as determined in Table 1, 2, or 3 • **All other indications:** 12 months or for duration supported in FDA label or compendia whichever is shorter **Table 1: Sovaldi + PEG-IFN + RBV Treatment Recommendations based on FDA labeling** **Genotype*** | **FDA labeled 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 labeled 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 |

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.

