Clinical Policy: Peginterferon Alfa-2a (Pegasys)

Reference Number: CP.PHAR.89
Effective Date: 10.11
Last Review Date: 08.23
Line of Business: Commercial, HIM, Medicaid

Revision Log

See Important Reminder at the end of this policy for important regulatory and legal information.

Description

Peginterferon alfa-2a (Pegasys®) is a covalent conjugate of recombinant alfa-2a interferon.

FDA Approved Indication(s)

Pegasys is indicated for the treatment of:

- Chronic hepatitis C (CHC) as part of a combination regimen with other hepatitis C virus (HCV) antiviral drugs in adult patients with compensated liver disease
- CHC as monotherapy in adult patient that have contraindication to or significant intolerance to other HCV antiviral drugs
- CHC in combination with ribavirin in pediatric patients 5 years of age and older with compensated liver disease
- Adult patients with HBeAg positive and HBeAg negative chronic hepatitis B (CHB) infection who have compensated liver disease and evidence of viral replication and liver inflammation
- HBeAg-positive CHB in non-cirrhotic pediatric patients 3 years of age and older with evidence of viral replication and elevations in serum alanine aminotransferase (ALT)

Limitation(s) of use:

- Pegasys alone or in combination with ribavirin without additional HCV antiviral drugs is not recommended for treatment of patients with CHC who previously failed therapy with an interferon-alfa
- Pegasys is not recommended for treatment of patients with CHC who have had solid organ transplantation

Policy/Criteria

Provider must submit documentation (such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria.

It is the policy of health plans affiliated with Centene Corporation® that Pegasys is **medically necessary** when the following criteria are met:

I. Initial Approval Criteria

A. NCCN-Recommended Off-Label Indications (off-label) (must meet all)**:**

1. Diagnosis of one of the following (a-k):
   a. One of the following myeloproliferative neoplasms (i, ii, or iii):
      i. Myelofibrosis, low risk and symptomatic;
      ii. Polycythemia vera;

iii. Essential thrombocythemia;
b. Systemic mastocytosis;
c. Hairy cell leukemia, prescribed as a single agent;
d. Erdheim-Chester disease;
e. Primary cutaneous CD30+ T-cell lymphoproliferative disorder;
f. Adult T-cell leukemia or lymphoma and prescribed in combination with zidovudine;
g. Mycosis fungoides or Sézary syndrome;
h. Chronic myeloid leukemia, during pregnancy;
2. Prescribed by or in consultation with an oncologist;
3. For Erdheim-Chester disease, used as a single agent for disease that is either symptomatic or relapsed/refractory;
4. Request meets one of the following (a or b):*
   a. Dose does not exceed 3 mcg/kg per week;
   b. Dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (*prescriber must submit supporting evidence*).

**Prescribed regimen must be FDA-approved or recommended by NCCN.*

Approval duration: 6 months

B. Chronic Hepatitis C Infection

1. Interferon-based treatment regimens are no longer recommended as of the 2018 American Association for the Study of Liver Diseases/ Infectious Disease Society of America (AASLD-IDSA) HCV guidance due to the advent of safe and effective direct acting antivirals *(see Appendix D)*.

Approval duration: Not applicable

C. Chronic Hepatitis B Infection (must meet all)**:**

1. Diagnosis of chronic hepatitis B virus infection;
2. Prescribed by or in consultation with gastroenterologist, hepatologist, or infectious disease specialist;
3. Meets ONE of the following (a, b, or c):
   a. Two elevated ALT lab values within the past 12 months (≥ 70 IU/L for men, ≥ 50 IU/L for women) and HBV DNA levels ≥ 20,000 IU/mL in HBeAg positive members or > 2,000 IU/mL in HBeAg negative members;
   b. Diagnosis of cirrhosis, HBV DNA level > 2,000 IU/mL, and age ≥ 18 years;
   c. Liver biopsy shows moderate/severe necroinflammation (Grade 9-18) or significant fibrosis (Stage 3-4);
4. Age ≥ 3 years;
5. If age ≤ 17 years, member does not have cirrhosis;
6. Dose does not exceed 180 mcg per week.

Approval duration: 48 weeks

D. Other diagnoses/indications (must meet 1 or 2)**:**

1. If this drug has recently (within the last 6 months) undergone a label change (e.g., newly approved indication, age expansion, new dosing regimen) that is not yet reflected in this policy, refer to one of the following policies (a or b):

a. For drugs on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the no coverage criteria policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.33 for health insurance marketplace, and CP.PMN.255 for Medicaid; or
b. For drugs NOT on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the non-formulary policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.103 for health insurance marketplace, and CP.PMN.16 for Medicaid; or

2. If the requested use (e.g., diagnosis, age, dosing regimen) is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized) AND criterion 1 above does not apply, refer to the off-label use policy for the relevant line of business: CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace, and CP.PMN.53 for Medicaid.

II. Continued Therapy

A. All Indications in Section I except CHC (must meet all):

1. Currently receiving medication via Centene benefit, or documentation supports that member is currently receiving Pegasys for a covered indication and has received this medication for at least 30 days;
2. Member is responding positively to therapy;
3. If request is for a dose increase, request meets one of the following (a or b)*:
   a. New dose does not exceed 180 mcg per week;
   b. New dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (*prescriber must submit supporting evidence*).

**Prescribed regimen must be FDA-approved or recommended by NCCN.*

Approval duration: 12 months (up to 5 years total for melanoma; up to a total of 48 weeks for HBV)

B. Chronic Hepatitis C Infection

1. Interferon-based treatment regimens are no longer recommended as of the 2018 AASLD-IDSA HCV guidance due to the advent of safe and effective direct acting antivirals.

Approval duration: Not applicable

C. Other diagnoses/indications (must meet 1 or 2):

1. If this drug has recently (within the last 6 months) undergone a label change (e.g., newly approved indication, age expansion, new dosing regimen) that is not yet reflected in this policy, refer to one of the following policies (a or b):
   a. For drugs on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the no coverage criteria policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.33 for health insurance marketplace, and CP.PMN.255 for Medicaid; or
   b. For drugs NOT on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the non-formulary policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.103 for health insurance marketplace, and CP.PMN.16 for Medicaid; or

2. If the requested use (e.g., diagnosis, age, dosing regimen) is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized) AND criterion 1 above does not apply, refer to the off-label use policy for the relevant line of business: CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace, and CP.PMN.53 for Medicaid.

III. Diagnoses/Indications for which coverage is NOT authorized:

- **A.** Non-FDA approved indications, which are not addressed in this policy, unless there is sufficient documentation of efficacy and safety according to the off label use policies – CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace, and CP.PMN.53 for Medicaid or evidence of coverage documents;
- **B.** Treatment of CHC;
- **C.** Uncontrolled autoimmune hepatitis;
- **D.** Following heart, lung or kidney transplants;
- **E.** Members with previous history of drug or alcohol abuse who have not abstained for at least 3 months before starting therapy;
- **F.** To solely reduce the risk of developing hepatocellular carcinoma (HCC) in members with cirrhosis.

IV. Appendices/General Information

Appendix A: Abbreviation/Acronym Key

AASLD/IDSA: American Association for the Study of Liver Diseases/ Infectious Disease Society of America
CHB: chronic hepatitis B
CHC: chronic hepatitis C
FDA: Food and Drug Administration
HBeAg: hepatitis B e-antigen
HCV: hepatitis C virus
NCCN: national comprehensive cancer network

Appendix B: Therapeutic Alternatives

Not applicable

Appendix C: Contraindications/Boxed Warnings

- Contraindication(s):
  - autoimmune hepatitis; hepatic decompensation (Child-Pugh score > 6 [class B and C]); hypersensitivity, neonates/infants.
- Boxed warning(s): risk of serious disorders (may cause or aggravate fatal or life-threatening neuropsychiatric, autoimmune, ischemic, and infectious disorders).

Appendix D: General Information

- Per NCCN Drugs and Biologics Compendium, pegylated interferons have a category 2A rating for treatment of chronic myeloid leukemia, Erdheim-Chester disease, essential thrombocythemia, hairy cell leukemia, myelofibrosis, polycythemia vera, primary cutaneous lymphomas (mycosis fungoides/Sezary syndrome, primary cutaneous CD30+ T-cell lymphoproliferative disorders), systemic mastocytosis, and T-cell leukemia/lymphoma (adult).
- Patients who develop anemia may be treated with epoetin to ensure that 80% of the original ribavirin dose is maintained throughout the course of therapy.

- According to the American Association for the Study of Liver Diseases (AASLD) the upper limit of normal for serum ALT concentrations for men and women are 35 IU/L and 25 IU/L, respectively.
- Grading and staging a liver biopsy for chronic hepatitis patients are as follows:
  - The grade is given a number based on the amount of inflammation (Knodell Scoring System).
    0 = no inflammation
    1-4 = minimal inflammation
    5-8 = mild inflammation
    9-12 = moderate inflammation
    13-18 = marked inflammation
  - The stage is scored based on the amount of fibrosis or scarring (Metavir Scoring System).
    0 = no scarring
    1 = minimal scarring
    2 = scarring has occurred and is outside the areas of the liver which include blood vessels
    3 = bridging fibrosis
    4 = cirrhosis or advanced scarring of the liver
- As of 2018, the AASLD/IDSA Hepatitis C treatment guidelines do not recommend treatment of CHC with PEG-interferon as this treatment has been superseded by treatments incorporating direct-acting antiviral agents and should not be used.
- 2018 AASLD technical remarks on peginterferon: contraindicated in persons with autoimmune disease, uncontrolled psychiatric disease, cytopenia, severe cardiac disease, uncontrolled seizures, and decompensated cirrhosis.
- According to the AASLD 2018 guidelines: Chronic Hepatitis B (CHB): Subdivided into HBeAg positive and negative. HBV-DNA levels are typically > 20,000 IU/mL in HBeAg-positive CHB, and lower values (2,000-20,000 IU/mL) are often seen in HBeAg-negative CHB. CHB therapy is recommended for persons with immune-active CHB and cirrhosis if HBV DNA is > 2,000 IU/mL, regardless of ALT level.

V. Dosage and Administration

Drug Name	Indication	Dosing Regimen	Maximum Dose
Peginterferon alfa-2a (Pegasys)	CHB infection	Adults: 180 mcg SQ per week as monotherapy for 48 weeks Pediatrics: 180 mcg/1.73 m^2 x BSA per week as monotherapy for 48 weeks	180 mcg per week

VI. Product Availability

- Vial: 180 mcg/mL
- Prefilled syringe: 180 mcg/0.5 mL (4 syringes/pack)

VII. References

1. Pegasys Prescribing Information. South San Francisco, CA: Genentech USA, Inc, March 2021. Available at: https://www.gene.com/download/pdf/pegasys_prescribing.pdf. Accessed April 21, 2023.
2. Peginterferon alfa-2a. In: National Comprehensive Cancer Network Drugs and Biologics Compendium. Available at: http://www.nccn.org/professionals/drug_compendium. Accessed April 21, 2023.
3. American Association for the Study of Liver Diseases/ Infectious Disease Society of America (AASLD-IDSA). HCV guidance: recommendations for testing, managing, and treating hepatitis C. Last updated October 24, 2022. Available at: https://www.hcvguidelines.org/. Accessed May 5, 2023.
4. Silver RT, Kiladjian JJ, Hasselbalch HC. Interferon and the treatment of polycythemia vera, essential thrombocythemia and myelofibrosis. Expert Review of Hematology 2013; 6(1):49-58. DOI: 10.1586/ehm.12.69.
5. Terrault NA, Lok ASF, McMahon BJ, et al. Update on Prevention, Diagnosis, and Treatment of Chronic Hepatitis B: AASLD 2018 Hepatitis B Guidance. Hepatology. 2018; 67 (4):1560-99.

Coding Implications

Codes referenced in this clinical policy are for informational purposes only. Inclusion or exclusion of any codes does not guarantee coverage. Providers should reference the most up-to-date sources of professional coding guidance prior to the submission of claims for reimbursement of covered services.

HCPCS Codes	Description
J3590	Unclassified biologics
S0145	Injection, peglated interferon alfa-2a, 180 mcg per mL

Reviews, Revisions, and Approvals	Date	P&T Approval Date
3Q 2019 annual review: added NCCN Compendium supported use in systemic mastocytosis; modified ALT requirements for CHB from 60/38 IU/L to 70/50 IU/L for men/women to align with AASLD recommendations for the upper limit of normal value used to guide treatment management decisions; references reviewed and updated.	05.14.19	08.19
3Q 2020 annual review: added systemic mastocytosis with associated hematologic malignancy, aggressive systemic mastocytosis, osteopenia or osteoporosis with refractory bone pain and/or decreasing bone mineral density on bisphosphonate therapy as per NCCN compendium; added specialist involvement for chronic hepatitis B infection; specified myelofibrosis as low risk and symptomatic as per NCCN compendium; updated chronic hepatitis B criteria to include >2,000 IU/mL in HBeAg negative	07.27.20	08.20

Reviews, Revisions, and Approvals	Date	P&T Approval Date
patients and HBV DNA level >2,000 IU/mL; updated Appendix D; references reviewed and updated.		
Added inadequate response or loss of response to hydroxyurea or interferon therapy if peginterferon alfa-2b or peginterferon alfa-2a naïve for polycythemia vera; added inadequate response or loss of response to hydroxyurea, anagrelide, or interferon therapy, if peginterferon alfa-2b or peginterferon alfa-2a naïve for essential thrombocytopenia; added NCCN-recommended (with Category 2A or above) off-label uses: primary cutaneous CD30+ T-cell lymphoproliferative disorder, adult T-cell leukemia or lymphoma; Mycosis fungoides or Sezary syndrome; added HCPCS codes; NCCN references reviewed and updated.	10.20.20	11.20
3Q 2021 annual review: Pegasys autoinjector discontinued and removed from section V; approval duration for melanoma and NCCN-supported off-label uses standardized to 6 months initial duration and 12 months continued duration; added off-label indications of hairy cell leukemia and Erdheim-Chester disease and corrected essential thrombocytopenia to essential thrombocythemia per NCCN; references for HIM line of business off-label use revised from HIM.PHAR.21 to HIM.PA.154; references reviewed and updated.	05.16.21	08.21
3Q 2022 annual review: removed Sylatron brand and corresponding melanoma criteria from policy as it has been discontinued with a Medispan obsolete date of 09/28/2021; per NCCN the following changes were made: added chronic myeloid leukemia off-label indication and updated Erdheim-Chester disease, essential thrombocythemia, polycythemia vera, and systemic mastocytosis off-label indications; clarified Pegasys maximum dosing for CHB is 180 mcg/week; references reviewed and updated.	07.20.22	08.22
Template changes applied to other diagnoses/indications.	10.12.22	
3Q 2023 annual review: removed PegIntron brand from policy as it has been discontinued with a Medispan obsolete date of 6/27/2023; removed minimum age of 5 years criterion from NCCN off-label oncology indications as Pegasys is indicated for peds as young as 3 years per PI-labeled indication; removed osteopenia/osteoporosis off-label indication as this is a complication of systemic mastocytosis; clarified that myelofibrosis, polycythemia vera, and essential thrombocythemia are myeloproliferative neoplasms; added off-label NCCN-supported criterion for use in combination with zidovudine in adult T-cell leukemia or lymphoma; removed hairy cell leukemia criterion for use following initial treatment with cladribine or pentostatin per NCCN; references reviewed and updated.	04.21.23	08.23

Important Reminder

This clinical policy has been developed by appropriately experienced and licensed health care professionals based on a review and consideration of currently available generally accepted standards of medical practice; peer-reviewed medical literature; government agency/program approval status; evidence-based guidelines and positions of leading national health professional organizations; views of physicians practicing in relevant clinical areas affected by this clinical policy; and other available clinical information. The Health Plan makes no representations and accepts no liability with respect to the content of any external information used or relied upon in developing this clinical policy. This clinical policy is consistent with standards of medical practice current at the time that this clinical policy was approved. "Health Plan" means a health plan that has adopted this clinical policy and that is operated or administered, in whole or in part, by Centene Management Company, LLC, or any of such health plan's affiliates, as applicable.

The purpose of this clinical policy is to provide a guide to medical necessity, which is a component of the guidelines used to assist in making coverage decisions and administering benefits. It does not constitute a contract or guarantee regarding payment or results. Coverage decisions and the administration of benefits are subject to all terms, conditions, exclusions and limitations of the coverage documents (e.g., evidence of coverage, certificate of coverage, policy, contract of insurance, etc.), as well as to state and federal requirements and applicable Health Plan-level administrative policies and procedures.

This clinical policy is effective as of the date determined by the Health Plan. The date of posting may not be the effective date of this clinical policy. This clinical policy may be subject to applicable legal and regulatory requirements relating to provider notification. If there is a discrepancy between the effective date of this clinical policy and any applicable legal or regulatory requirement, the requirements of law and regulation shall govern. The Health Plan retains the right to change, amend or withdraw this clinical policy, and additional clinical policies may be developed and adopted as needed, at any time.

This clinical policy does not constitute medical advice, medical treatment or medical care. It is not intended to dictate to providers how to practice medicine. Providers are expected to exercise professional medical judgment in providing the most appropriate care, and are solely responsible for the medical advice and treatment of members. This clinical policy is not intended to recommend treatment for members. Members should consult with their treating physician in connection with diagnosis and treatment decisions.

Providers referred to in this clinical policy are independent contractors who exercise independent judgment and over whom the Health Plan has no control or right of control. Providers are not agents or employees of the Health Plan.

This clinical policy is the property of the Health Plan. Unauthorized copying, use, and distribution of this clinical policy or any information contained herein are strictly prohibited. Providers, members and their representatives are bound to the terms and conditions expressed herein through the terms of their contracts. Where no such contract exists, providers, members

and their representatives agree to be bound by such terms and conditions by providing services to members and/or submitting claims for payment for such services.

Note: For Medicaid members, when state Medicaid coverage provisions conflict with the coverage provisions in this clinical policy, state Medicaid coverage provisions take precedence. Please refer to the state Medicaid manual for any coverage provisions pertaining to this clinical policy.