Clinical Policy Title:	peginterferon alfa-2a, b
Policy Number:	RxA.248
Drug(s) Applied:	Pegasys®, PegIntron®
Original Policy Date:	02/07/2020
Last Review Date:	06/10/2021
Line of Business Policy Applies to:	All lines of business

Background

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

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).

PegIntron® is indicated for treatment of CHC in patients with compensated liver disease.

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.

Dosing Information

Drug Name	Indication	Dosing Regimen	Maximum Dose
peginterferon alfa-2b (PegIntron®)	CHC	Adults: 1.5 mcg/kg/ week Pediatrics: 60 mcg/m^2/ week	Adults: 1.5 mcg/kg/ week Pediatrics: 60 mcg/m^2/ week
peginterferon alfa-2a (Pegasys®)	CHB	Adults: 180 mcg per week for 48 weeks Pediatrics: 180 mcg/1.73 m^2 × BSA per week for 48 weeks	Adults: 180 mcg per week Pediatrics: 180 mcg/1.73 m^2 x BSA per week

Dosing Information

Drug Name	Indication	Dosing Regimen	Maximum Dose
peginterferon alfa-2a (Pegasys®)	CHC	Adults: 180 mcg SC per week as monotherapy Pediatrics: 180 mcg/1.73 m^2 x BSA per week as monotherapy	Adults: 180 mcg per week Pediatrics: 180 mcg/1.73 m^2 x BSA per week

Dosage Forms

- Peginterferon alfa-2a (Pegasys®):
  - Vials: 180 mcg/mL
  - Prefilled syringes: 180 mcg/0.5 mL (4 syringes/pack)
  - Autoinjector: 135 mcg/0.5 mL, 180 mcg/0.5 mL
- Peginterferon alfa-2b (PegIntron®):
  - Vials (with diluent)
  - Redipen: 50 mcg/0.5 mL, 80 mcg/0.5 mL, 120 mcg/0.5 mL, 150 mcg/0.5 mL

Clinical Policy

Provider must submit documentation (such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria. The provision of provider samples does not guarantee coverage under the terms of the pharmacy benefit administered by RxAdvance. All criteria for initial approval must be met in order to obtain coverage.

I. Initial Approval Criteria

A. Chronic Hepatitis C

Interferon-based treatment regimens are no longer recommended by the 2017 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.

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

1. Diagnosis of chronic hepatitis B virus infection;
2. Request is for Pegasys®;
3. Meets one of the following:
   a. Two elevated ALT lab values within the past 12 months (e.g., 70 IU/L or greater for men, 50 IU/L or greater for women) and HBV DNA levels 20,000 IU/ml or greater;
   b. Diagnosis of cirrhosis and member is 18 years of age or older;
   c. Liver biopsy shows moderate/severe necroinflammation (Grade 9-18) or significant fibrosis (Stage 3-4);
4. Member is 3 years of age or older;
5. If age 17 years or age or younger, member does not have cirrhosis;
6. Dose does not exceed 180 mcg per week for adults or 180 mcg/1.73 m^2 x BSA per week for pediatric patients.

Approval Duration

Commercial: 12 months

Medicaid: 12 months

C. Erdheim-Chester Disease (off-label) (must meet all):
1. Diagnosis of Erdheim-Chester Disease (ECD);
2. Request is for Pegasys® or PegIntron®;
3. Pegasys® or PegIntron® is used as a preferred first-line or subsequent therapy, irrespective of mutation, as single agent for ECD with symptomatic disease or relapsed/refractory disease;
4. Prescribed by or in consultation with an oncologist;
5. Member is 18 years of age or older;
6. 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
Commercial: 12 months
Medicaid: 12 months

D. Hairy Cell Leukemia (off-label) (must meet all):
1. Diagnosis of Hairy Cell Leukemia;
2. Request is for Pegasys®;
3. Prescribed by or in consultation with an oncologist;
4. Member is 18 years of age or older;
5. Pegasys® is used a single agent for (a or b):
   a. less than complete response following initial treatment with cladribine or pentostatin; or
   b. relapse within 2 years of complete response;
6. 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
Commercial: 12 months
Medicaid: 12 months

E. Myeloproliferative Neoplasms, Systemic Mastocytosis (off-label) (must meet all):
1. Diagnosis of one of the following (a, b, c, or d):
   a. Myelofibrosis;
   b. Polycythemia vera;
   c. Essential thrombocytopenia;
   d. Systemic mastocytosis;
2. Prescribed by or in consultation with an oncologist;
3. Member meets one of the following:
   a. For PegIntron®: Member is 3 years of age or older;
   b. For Pegasys®: Member is 5 years of age or older;
4. Request meets one of the following (a or b):
   a. Dose does not exceed (i or ii):
      i. For PegIntron®: 1.5 mcg/kg/week;
      ii. For Pegasys®: 3 mcg/kg/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
Commercial: 12 months
Medicaid: 12 months

F. Primary Cutaneous Lymphomas (off-label) (must meet all):

1. Diagnosis of Primary Cutaneous Lymphomas (a, b, or c):
   a. Primary Cutaneous CD30+ T-Cell Lymphoproliferative Disorders
   b. Mycosis Fungoides/Sezary Syndrome
   c. Adult T-Cell Leukemia/Lymphoma
2. Request is for Pegasys®;
3. Prescribed by or in consultation with an oncologist;
4. Member is 18 years of age or older;
5. Pegasys® is prescribed as a substitute for other interferon preparations;
6. Request meets one of the following (a or b):
   a. Dose does not exceed initial dose of 360 mcg once weekly;
   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
Commercial: 12 months
Medicaid: 12 months

II. Continued Therapy Approval

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

1. Member is currently receiving medication that has been authorized by RxAdvance, or documentation supports that member is currently receiving Pegasys® or PegIntron® 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 (i or ii):
      i. PegIntron®: 1.5 mcg/kg per week;
      ii. Pegasys®: 180 mcg per week for adults and 180 mcg/1.73 m2 x BSA per week for pediatric patients;
   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
Commercial: 12 months
Medicaid: 12 months

B. Chronic Hepatitis C:
Interferon-based treatment regimens are no longer recommended by the AASLD-IDSA HCV guidance due to the advent of safe and effective direct acting antivirals.

III. Appendices

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

APPENDIX B: Therapeutic Alternatives
Not applicable

APPENDIX C: Contraindications/Boxed Warnings

- Contraindication(s):
  - Pegasys® and PegIntron®: autoimmune hepatitis; hepatic decompensation (Child-Pugh score > 6 [class B and C]); hypersensitivity reactions, such as urticaria, angioedema, anaphylaxis, bronchoconstriction, Stevens-Johnson syndrome, and toxic epidermal necrolysis.
  - Pegasys®: neonates/infants

- Boxed Warning(s):
  - Risk of serious disorders (may cause or aggravate fatal or life threatening neuropsychiatric, depression autoimmune, ischemic, and infectious disorders).

APPENDIX D: General Information

- According to FDA approved labeling, recent evidence supports dose reduction of pegylated interferon for neutropenic hepatitis C patients treated with combination therapy (pegylated interferon and ribavirin). Treatment with filgrastim is not FDA approved or recommended according to current hepatitis C treatment guidelines.
- 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
- 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.

References

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Review/Revision History	Review/Revision Date	P&T Approval Date
Policy established.	01/2020	02/07/2020
Policy was reviewed: 1. Policy title table was updated: Clinical Policy Title was updated to "peginterferon alfa-2a, b"; Drug(s) Applied was updated to "Pegasys®, PegIntron®, Sylatron™; Line of Business Policy Applies to was updated to "All". 2. Clinical policy was updated: Approval duration was updated for both Initial and Continued Approval Criteria; Continued Approval was rephrased to "Currently receiving medication that has been authorized by RxAdvance….". 3. Contraindication (appendix C) was updated: “Risk of serious disorders (may cause or aggravate fatal or life threatening neuropsychiatric, depression autoimmune, ischemic, and infectious disorders)”. 4. References were updated.	08/01/2020	09/14/2020
Policy was reviewed: 1. Clinical Policy title was updated. 2. Dosing Information was updated. 3. Initial Approval Criteria for approval updated along with the addition of other off label indications. 4. Initial duration of approval updated. 5. Continued Therapy criteria II.A.1 was rephrased to "Member is currently receiving medication that has been authorized by RxAdvance..." 6. References were reviewed and updated.	03/03/2021	06/10/2021