RXADVANCE
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Clinical Policy Title:	peginterferon alfa-2a,b
Policy Number:	RxA.248
Drug(s) Applied:	Pegasys®, PegIntron®, Sylatron™
Original Policy Date:	02/07/2020
Last Review Date:	09/14/2020
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®, Sylatron™) 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.
Sylatron™ is indicated for the adjuvant treatment of melanoma with microscopic or gross nodal involvement within 84 days of definitive surgical resection including complete lymphadenectomy.

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®, Sylatron™)	Myelofibrosis, polycythemia vera, Essential thrombocytopenia	30 mcg/week SC with dose titration upward as tolerated	N/A
Peginterferon alfa-2b (Sylatron™)	Melanoma	6 mcg/kg/week SC for 8 doses, followed by 3 mcg/kg/week SC for up to 5 years	6 mcg/kg/week for the first 8 doses 3 mcg/kg/week for up to 5 years
Peginterferon alfa-2a (Pegasys®)	Chronic hepatitis B infection	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
	Myelofibrosis	Dose varies: 2-3 mcg/kg SC/week	Treatment continues until no longer clinically beneficial or until unacceptable toxicity occurs

Dosage Forms	
Drug	**Availability**
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
Peginterferon alfa-2b (Sylatron™)	Single-use vials: 200 mcg/0.5 mL, 300 mcg/0.5 mL, 600 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.

I. Initial Approval Criteria

A. Melanoma (must meet all):

1. Diagnosis of melanoma;

2. Request is for Sylatron™;
3. Prescribed by or in consultation with an oncologist;
4. Age ≥ 18 years;
5. Request meets one of the following (a or b):
    a. Dose does not exceed initial dose of: 6 mcg/kg per week for 8 weeks, then 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*).

Approval Duration
Commercial: 16 months
Medicaid: 6 months
HIM: 6 months

B. 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 Sylatron™: age ≥ 18 years;
    b. For PegIntron®: age ≥ 3 years;
    c. For Pegasys®: age ≥ 5 years;
4. Request meets one of the following (a or b):
    a. Dose does not exceed (i, ii, or iii):
        i. For PegIntron®: 1.5 mcg/kg/week;
        ii. For Sylatron™: 6 mcg/kg/week;
        iii. 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).

Approval Duration
Commercial: 6 months
Medicaid: 6 months
HIM: 6 months

C. 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.

D. 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 ((≥ 70 IU/L for men, ≥ 50 IU/L for women) and HBV DNA levels ≥ 20,000 IU/ml;
    b. Diagnosis of cirrhosis 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 for adults and 180 mcg/1.73 m^2 x BSA per week for pediatric patients.

Approval Duration
Commercial: 12 months
Medicaid: 12 months
HIM: 12 months

II. Continued Therapy Approval

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

1. Currently receiving medication that has been authorized by RxAdvance, or documentation supports that member is currently receiving Pegasys®, PegIntron®, or Sylatron™ 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, ii, or iii):
        i. PegIntron®: 1.5 mcg/kg per week;
        ii. Sylatron™: 6 mcg/kg/week for 8 weeks, then 3 mcg/kg per week;
        iii. Pegasys®: 180 mcg per week for adults and 180 mcg/1.73 m2 x BSA per week for pediatric patients;
    b. New dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (prescriber must submit supporting evidence).

Approval Duration
Commercial: 12 months
Medicaid: 12 months
HIM: 12 months

B. Chronic Hepatitis C:
Interferon-based treatment regimens are no longer recommended by the AASLDIDSA 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®, PegIntron®, and Sylatron™: autoimmune hepatitis; hepatic decompensation (Child-Pugh

score > 6 [class B and C]); hypersensitivity
- 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 Neupogen 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/Revised 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