UnitedHealthcare Community Plan

Clinical Pharmacy Program Guidelines for Alfa Interferons

Program	Prior Authorization
Medication	Intron® A (interferon alfa-2b), Pegasys® (peginterferon alfa-2a), PegIntron® and Sylatron™ (peginterferon alfa-2b)
Markets in Scope	California,Colorado,Hawaii, Maryland, Nevada, New Jersey, New York, New York EPP, Pennsylvania- CHIP, Rhode Island, South Carolina
Issue Date	9/2009
Pharmacy and Therapeutics Approval Date	11/2020
Effective Date	12/2020

1. Background:

Indications

Intron A (interferon alfa-2b) is indicated for the treatment of chronic hepatitis C in patients 18 years of age or older with compensated liver disease who have a history of blood or blood-product exposure and/or are HCV antibody positive. Intron A has additional FDA labeling for the treatment of chronic hepatitis C in patients 3 years of age and older with compensated liver disease previously untreated with alpha interferon therapy and in patients 18 years of age and older who have relapsed following alpha interferon therapy. Intron A is also indicated for the treatment of chronic hepatitis B in patients 1 year of age or older with compensated liver disease. Patients who have been serum HBsAg positive for at least 6 months and have evidence of HBV replication (serum HBeAg positive) with elevated serum ALT are candidates for treatment. Intron A is indicated for the treatment of patients 18 years of age or older with hairy cell leukemia. Intron A is indicated as adjuvant to surgical treatment in patients 18 years of age or older with malignant melanoma who are free of disease but a high risk for systemic recurrence, within 56 days of surgery. It is also indicated for the initial treatment of clinically aggressive follicular Non-Hodgkin's lymphoma in conjunction with anthracycline-containing combination chemotherapy in patients 18 years of age or older. Intron A is indicated for intralesional treatment of selected patients 18 years of age or older with condylomata acuminata involving external surfaces of the genital and perianal areas. It is also indicated for the treatment of selected patients 18 years of age or older with AIDS-Related Kaposi's Sarcoma.[1]

The National Comprehensive Cancer Network (NCCN) also recommends use of Intron A for myeloproliferative neoplasms (MPNs) such as essential thrombocytopenia (ET), polycythemia vera (PV), and primary myelofibrosis (PM), adult T-cell leukemia / lymphoma, mycosis fungoides / Sézary syndrome, and systemic mastocytosis.[2]

Pegasys (peginterferon alfa-2a) is an antiviral indicated for the treatment of chronic hepatitis C (CHC) as part of a combination regimen with other hepatitis C virus (HCV) antiviral drugs in patients 5 years of age and older with compensated liver disease. Pegasys monotherapy is indicated for CHC only if patient has contraindication to or significant intolerance to other HCV antiviral drugs. Pegasys is indicated in the treatment of adult patients with HBeAg positive and HBeAg negative chronic hepatitis B infection who have compensated liver disease and evidence of viral replication and liver inflammation. [3]

PegIntron (peginterferon alfa-2b), as part of a combination regimen, is indicated for the treatment of chronic hepatitis C in patients with compensated liver disease. PegIntron monotherapy should only be used in the treatment of CHC in patients with compensated liver disease if there are contraindications to or significant intolerance of ribavirin and is indicated for use only in previously untreated adult patients.[4]

The National Comprehensive Cancer Network (NCCN) also recommends the use of peginterferon alfa-2a in patients with myeloproliferative neoplasms (MPNs) such as essential thrombocytopenia (ET), polycythemia vera (PV), and primary myelofibrosis (PM), and systemic mastocytosis, as well as mycosis fungoides/Sezary syndrome, hairy cell leukemia, primary cutaneous CD30+ T-cell lymphoproliferative disorders, and adult T-cell leukemia/lymphoma.

Another formulation of peginterferon alfa-2b, Sylatron, is FDA approved for the adjuvant treatment of malignant melanoma with microscopic or gross nodal involvement within 84 days of definitive surgical resection including complete lymphadenectomy.[5]

2. Coverage Criteria:

A. <u>Treatment of Hepatitis B</u>

1. **Intron A, Pegasys, or PegIntron** will be approved based on **<u>all</u>** of the following criteria:

   a. Chronic Hepatitis B infection

   -AND-

   b. Patient without decompensated liver disease*

   Authorization will be issued for 48 weeks.

   *Defined as Child-Pugh Class B or C

B. <u>Treatment of Chronic Hepatitis C (Intron A, Pegasys and PegIntron)</u>

1. **Intron A, Pegasys or PegIntron as part of a combination antiviral treatment regimen**

   a. **Intron A, Pegasys, or PegIntron** will be approved based on **all** of the following criteria:

      (1) Diagnosis of chronic hepatitis C infection

      -AND-

      (2) Patient without decompensated liver disease*

      -AND-

      (3) Will be used as part of a combination antiviral treatment regimen

   Authorization will be issued for 48 weeks.

   *Defined as Child-Pugh Class B or C

C. **For Diagnoses Other Than Hepatitis**

1. **PegIntron** will be approved based on one of the following diagnoses:

   a. For the treatment of myeloproliferative neoplasms (MPNs) such as essential thrombocythemia (ET), polycythemia vera (PV), or primary myelofibrosis (PM)

   -OR-

   b. Systemic mastocytosis

   Authorization will be issued for 12 months.

2. **Sylatron** will be approved based on **one** of the following diagnoses:

   a. Malignant melanoma

   -OR-

   b. For the treatment of myeloproliferative neoplasms (MPNs) such as essential thrombocythemia (ET), polycythemia vera (PV), or primary myelofibrosis (PM)

   -OR-

c. Systemic mastocytosis

Authorization will be issued for 12 months.

3. **Intron A** will be approved based on **one** of the following diagnoses:

a. Hairy cell leukemia
b. Condylomata acuminata (genital or perianal)
c. AIDS-related Kaposi's sarcoma
d. For the treatment of myeloproliferative neoplasms (MPNs) such as essential thrombocythemia (ET), polycythemia vera (PV), or primary myelofibrosis (PM)
e. Follicular lymphoma
f. Adult T-cell leukemia / lymphoma
g. Mycosis fungoides / Sézary syndrome
h. Malignant Melanoma
i. Systemic mastocytosis

Authorization will be issued for 12 months.

. 4. **Pegasys** will be approved based on **one** of the following diagnoses:

a. For the treatment of myeloproliferative neoplasms (MPNs) such as essential thrombocythemia (ET), polycythemia vera (PV), or primary myelofibrosis (PM)
b. Systemic mastocytosis
c. Hairy cell leukemia
d. Mycosis fungoides/Sezary syndrome
e. Primary cutaneous CD30+ T-cell lymphoproliferative disorders
f. Adult T-cell leukemia/lymphoma

D. NCCN Recommended Regimens

1. Initial Authorization

a. **Intron A, Pegasys, PegIntron, or Sylatron** will be approved for uses not outlined above if supported by The National Comprehensive Cancer Network (NCCN) Drugs and Biologics Compendium.

Authorization will be issued for 12 months.

2. Reauthorization

a. **Intron A, Pegasys, PegIntron, or Sylatron** will be approved based on the following criterion:

(1) Documentation of positive clinical response to Intron A, Pegasys, PegIntron, or Sylatron therapy

Authorization will be issued for 12 months.

3. Additional Clinical Rules:

- Notwithstanding Coverage Criteria, UnitedHealthcare may approve initial and re-authorization based solely on previous claim/medication history, diagnosis codes (ICD-10) and/or claim logic. Use of automated approval and re-approval processes varies by program and/or therapeutic class.
- Supply limits may be in place.

4. References:

1. Intron A [package insert]. Whitehouse Station, NJ: Merck & Co., Inc.; August 2019.
2. The NCCN Drugs and Biologics Compendium (NCCN Compendium™). Accessed October 6, 2020 at http://www.nccn.org/professionals/drug_compendium/content/contents.asp
3. Pegasys [package insert]. South San Francisco, CA: Genentech USA, Inc.; October 2017.
4. PegIntron [package insert]. Whitehouse Station, NJ: Merck & Co., Inc.; August 2019.
5. Sylatron [package insert]. Whitehouse Station, NJ: Merck & Co., Inc.; August 2019.
6. Kiladjian JJ, Cassinat B, Turlure P, et al. High molecular response rate of polycythemia vera patients treated with pegylated interferon alpha-2a. Blood. 2006 Sep15;108(6):2037-40.
7. Kiladjian JJ, Cassinat B, Chevret S, et al. Pegylated interferon-alfa-2a induces complete hematologic and molecular responses with low toxicity in polycythemia vera. Blood. 2008 Oct 15;112(8):3065-72.
8. Quintás-Cardama A, Kantarjian H, Manshouri T, et al. Pegylated interferon alfa-2a yields high rates of hematologic and molecular response in patients with advanced essential thrombocythemia and polycythemia vera. J Clin Oncol. 2009 Nov 10;27(32):5418-24.
9. Ianotto JC, Kiladjian JJ, Demory JL, et al. PEG-IFN-alpha-2a therapy in patients with myelofibrosis: a study of the French Groupe d'Etudes des Myelofibroses (GEM) and

France Intergroupe des syndromes Myéloprolifératifs (FIM). Br J Haematol. 2009 Jul;146(2):223-5.

Program	Prior Authorization - Intron® A (interferon alfa-2b), Pegasys® (peginterferon alfa-2a), PegIntron® and Sylatron™ (peginterferon alfa-2b)
Change Control	
Date	Change
9/2009	Criteria taken from previously approved AmeriChoice and Unison policy (RX06 Interferon Alfa 2a and 2b, Chronic Hepatitis C medications). Policy reformatted.
6/2010	Hepatitis C Added guidelines for Non-FDA approved indications: Acute Hepatitis C, Multiple Myeloma, Re-Treatment for Chronic Hepatitis C (Pegasys, PegIntron). Changed the "≥ 2 log decrease in HCV RNA level" re-authorization requirement to "HCV RNA test at 24 weeks of treatment was negative". Changed "patient has no contraindications to therapy with interferon/peginterferon" to "patient is without decompensated liver disease". Added "the patient is positive for HCV antibodies" to the guidelines. Included genotype 6 and HCV/HIV patients in the guidelines. Treatment duration for these groups is 48 weeks. Hepatitis B Added "evidence of active virus replication" and "evidence of active liver disease" to the guidelines. Removed re-authorization guidelines.
9/2010	Updated Hepatitis C guidelines to include criteria for re-treatment with Infergen monotherapy and Infergen/ribavirin combination therapy (for patients that failed to respond to pegylated interferon/ ribavirin therapy.
9/2011	Added Sylatron criteria to guideline
12/2011	Updated guideline to include criteria for triple therapy regimen including peginterferon and ribavirin used in combination with a HCV NS3/4A protease inhibitor. Section III.D.1 and III.D.2. Updated Ribavirin sections for dual therapy to include full criteria required for interferon products

2/2012	Updated age requirements for PegIntron and Pegasys in sections III.A.1.e and III.C.1.e. Updated age requirements for IntronA and Infergen in section III.A.2.e. Added an additional HCV-RNA level requirement for treatment naïve patients with cirrhosis who were on an Incivek regimen and are continuing peginterferon and ribavirin after triple therapy for 12 weeks. See section III.E.1.d.(1) and section III.E.2.d.(1).
9/2012	Peg-Intron moved to non-preferred drug column in the product list section (I. Benefit Coverage).
7/2013	Converted policy to new UHC enterprise wide formatting Complete reorganization of guideline down to the individual drug(s) and their indications. Full clinical re-review was completed to accomplish this. Removed Sylatron from this guideline. Removed Ribavirin from guideline and created individual ribavirin guideline
3/2014	▪ Removed the age criterion for all products and indications ▪ Added new criteria for Pegasys and Peg-Intron triple therapy (including Olysio). o Initial authorization criteria include: diagnosis of chronic hepatitis C genotype 1, being used in combination with Olysio and ribavirin, and prescribed by a hepatologist, gastroenterologist or infectious disease specialist. Peg-Intron criteria mirror Pegasys except for a criterion requiring documentation explaining the reason for failure or intolerance to the preferred product (Pegasys). o First reauthorization criteria include: HCV RNA < 25 IU/mL at treatment week 4, HCV RNA < 25 IU/mL at treatment week 12, used in combination with ribavirin, and prescribed by a hepatologist, gastroenterologist or infectious disease specialist. Authorization will be used for 8 weeks for the following patients: 1) treatment-naïve patients, including those with cirrhosis or 2) previous relapsers, including those with cirrhosis, to peginterferon alfa and ribavirin therapy. Authorization will be issued for an additional 12 weeks in the following patients: previous partial or null responders, including those with cirrhosis, to peginterferon alfa and ribavirin therapy. o Second authorization criteria include: HCV RNA < 25 IU/mL at treatment week 24 and used in combination with

	ribavirin. Authorization will be issued for an additional 20 weeks in the following patients: previous partial or null responders, including those with cirrhosis, to peginterferon alfa and ribavirin therapy. Treatment-naïve and prior relapser patients including those with cirrhosis complete treatment after 24 weeks and will not be approved for a second continuation of therapy. ▪ Added new criteria for Pegasys and Peg-Intron triple therapy (including Sovaldi). Criteria include: diagnosis of chronic hepatitis C genotype 1 or 4 infection, being used in combination with Sovaldi and ribavirin, without decompensated cirrhosis, prescribed by a hepatologist, gastroenterologist or infectious disease specialist, and chart documentation explaining the reason for failure or intolerance to Pegasys (only applies to Peg-Intron). Authorization will be issued for 12 weeks. ▪ Updated background information and references.
4/2015	Simplified and streamlined the entire alfa interferon criteria: ▪ Hepatitis B: all criteria sections for hepatitis B were combined and streamlined into a single section for Intron A and Pegasys ▪ Criteria sections for diagnoses other than hepatitis and condylomata acuminata were combined into a single criteria section addressing all diagnoses ▪ Hepatitis C: all hepatitis C sections were removed and simplified into a single criteria section for Pegasys requiring a diagnosis of hepatitis C and used in combination with Sovaldi or Olysio. Non-pegylated interferon sections have been removed due to AASDL recommendations for the treatment of hepatitis C. The following section remains unchanged: ▪ Intron A for Condylomata acuminata
11/2016	Updated clinical criteria to align with Employer and Individual's policy, including addition of Sylatron to this policy
11/2017	Updated off-label NCCN recommendations for use. Removed CML (Intron A, Pegasys, Pegintron) and systemic light chain amyloidosis (Intron A) indications as no longer rec by NCCN. Updated references.
11/2018	Annual review. Updated background and criteria to include NCCN recommended use for systemic mastocytosis. Updated references.
11/2019	Annual review. Added NCCN recommended regimen criteria. Updated references.
11/2020	Annual review. Updated background and criteria to include NCCN recommendations. Updated references. Added Additional Clinical Rules section.