Intron A

Description

Intron A (interferon alfa-2b)

Background
Interferons are a family of naturally-occurring proteins that are made and secreted by cells of the immune system (for example, white blood cells, natural killer cells, fibroblasts, and epithelial cells). Three classes of interferons have been identified: alpha, beta, and gamma (1).

Each class has many effects, though their effects overlap. Commercially available interferons are human interferons manufactured using recombinant DNA technology. The mechanism of action of interferon is complex and is not well understood. Interferons modulate the response of the immune system to viruses, bacteria, cancer, and other foreign substances that invade the body. Interferons do not directly kill viral or cancerous cells; they boost the immune system response and reduce the growth of cancer cells by regulating the action of several genes that control the secretion of numerous cellular proteins that affect growth (1).

Regulatory Status
FDA-approved indications: Intron A is an alpha interferon indicated for:

1. **Hairy Cell Leukemia**: Intron A is indicated for the treatment of patients 18 years of age or older with hairy cell leukemia (2).

2. **Malignant Melanoma**: 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 at high risk for systemic recurrence, within 56 days of surgery (2).
3. **Follicular Lymphoma:** Intron A is 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. Efficacy of Intron A therapy in patients with low-grade, low tumor burden follicular Non-Hodgkin’s Lymphoma has not been demonstrated (2).

4. **Condylomata Acuminata:** 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. The use of this product in adolescents has not been studied (2).

5. **AIDS-Related Kaposi’s Sarcoma:** Intron A is indicated for the treatment of selected patients 18 years of age or older with AIDS-Related Kaposi’s Sarcoma. The likelihood of response to Intron A therapy is greater in patients who are without systemic symptoms, who have limited lymphadenopathy and who have a relatively intact immune system as indicated by total CD4 count (2).

**Off-Label Uses:** (3 - 7)
1. Carcinoid tumor
2. Polycythemia vera
3. T-Cell Lymphomas - Mycosis Fungoides/Sézary Syndrome
4. Renal cell cancer

All alpha interferons, including Intron A, carry a boxed warning that they can cause or aggravate fatal or life-threatening neuropsychiatric, autoimmune, ischemic, and infectious disorders. Patients should be monitored closely with periodic clinical and laboratory evaluations. Patients with persistently severe or worsening signs or symptoms of these conditions should be withdrawn from therapy. In many but not all cases these disorders resolve after stopping Intron A therapy (2).

**Related policies**
Actimmune, Sylatron

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**Policy**

This policy statement applies to clinical review performed for pre-service (Prior Approval, Precertification, Advanced Benefit Determination, etc.) and/or post-service claims.

Intron A may be considered **medically necessary** in patients that are 18 years of age or older with a confirmed diagnosis of hairy cell leukemia, malignant melanoma, carcinoid tumor, polycythemia vera, follicular lymphoma, condylomata acuminata, renal cell carcinoma,
Cutaneous T-cell lymphomas including Mycosis Fungoides and Sezary Syndrome or AIDS-related Kaposi’s sarcoma.

Intron A may be considered investigational in patients that are below 18 years of age and for all other indications.

Prior-Approval Requirements

Age
18 years of age or older

Diagnoses

Patient must have ONE of the following:

1. AIDS-related Kaposi’s sarcoma
2. Carcinoid tumor
3. Condylomata acuminata
4. Follicular lymphoma
5. Hairy cell leukemia
6. Malignant melanoma
7. Polycythemia vera
8. Renal cell cancer
9. Cutaneous T-cell lymphoma (Mycosis Fungoides and Sezary Syndrome)

Prior – Approval Renewal Requirements

Same as above

Policy Guidelines

Pre - PA Allowance
None

Prior - Approval Limits
Duration 12 months

Prior – Approval Renewal Limits
Duration 12 months

Rationale
Summary
Interferons are naturally occurring proteins with antiviral, antiproliferative and immunoregulatory properties. They are produced and secreted in response to viral infections and to a variety of other synthetic and biological inducers. Three types of interferons have been identified: alpha, beta, and gamma. Binding of interferon to membrane receptors initiates a series of events including induction of protein synthesis. These actions are followed by a variety of cellular responses, including inhibition of virus replication and suppression of cell proliferation (1).

Prior authorization is required to ensure the safe, clinically appropriate and cost effective use of Intron A while maintaining optimal therapeutic outcomes.

References

Policy History
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<thead>
<tr>
<th>Date</th>
<th>Action</th>
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<tbody>
<tr>
<td>October 2004</td>
<td>Criteria updated to reflect current guidelines:</td>
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<tr>
<td></td>
<td>NIH Consensus Statement on Management of Hepatitis C: 2002</td>
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<td></td>
<td>NIH Consensus Statements and State-of-the-Science Statements</td>
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<tr>
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<td>Volume 19, Number 3, June 10-12, 2002</td>
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<tr>
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<td>National Institutes of Health, Office of the Director</td>
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<tr>
<td></td>
<td>Diagnosis, Management, and Treatment of Hepatitis C</td>
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<td>American Association for the Study of Liver Diseases</td>
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<td>Hepatology, April 2004</td>
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June 2009  Follicular lymphoma maintenance therapy added as a new indication for interferon therapy. The use of aggressive chemotherapy and maintenance therapy with interferon alpha-2b in follicular lymphoma improved outcome; more than 60% of patients remain alive, free of disease at longer follow-up.

July 2009  Criteria updated to remove Roferon, which has been discontinued by manufacturer.

March 2010  Intron A removed from the Interferon Therapy Criteria document and made into its own criteria document. Criteria documents reorganized by drug, rather than disease state, to improve functionality and prior authorization work flow.

March 2010  Diagnoses of hepatitis B and hepatitis C removed from Section 4 (Interferon Therapy) as they are now addressed in Section 1 (Hepatitis B), Section 2 (Hepatitis B Monotherapy) and Section 3 (Hepatitis C Combination Therapy CHILD) of this document. References to Actimmune and the diagnosis of osteopetrosis removed from Section 4 (Interferon Therapy) as they are currently addressed in the criteria document entitled Interferon Therapy Criteria, which addresses Actimmune and Alferon-N.

August 2011  Section 4 (Interferon Therapy) reviewed and revised as follows:
Currently Intron A is FDA labeled for the following indications: AIDS-related Kaposi’s sarcoma, condylomata acuminata, follicular lymphoma, hairy cell leukemia, malignant melanoma, and chronic hepatitis B and C. Chronic hepatitis B and C are addressed in sections 1/2/3 of the criteria. Chronic granulomatous disease and inflammatory pulmonary fibrosis removed from criteria due to either being an investigational use or no current clinical sources supporting its use. A review of the service plan’s Intron A approvals on appeal from 6/2010 through 6/2011 confirmed that the addition of carcinoid tumor, multiple myeloma, polycythemia vera, and renal cell cancer would be appropriate. It also confirmed that chronic myeloid leukemia needs to remain in the criteria.

August 2011  ICD-9 codes removed from all sections of the criteria.

September 2011  All clinical rationale and revision notes moved to the end of the document, cross referenced to their corresponding section, and placed in chronological order.
**Section:** Prescription Drugs

**Effective Date:** April 1, 2019

**Subsection:** Antineoplastic Agents

**Original Policy Date:** December 29, 2011

**Subject:** Intron A

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**November 2011**  
Section 4 (Interferon Therapy) added further requirements for the indication of CML. The standard of care in CML is the use of Tyrosine Kinase Inhibitors (TKIs) which have shown to be more efficacious in achieving both major and complete cytogenetic responses. Interferon therapy should be reserved only for patients that demonstrate intolerance of TKIs. Also clarified the definition of CML to include patients that are Philadelphia chromosome-negative but BCR-ABL positive. Limiting use of Intron A in patients with only Philadelphia chromosome-positive CML may in effect deprive patients of treatment. This also aligns the PA-requirements with the NCCN guidelines for CML diagnosis.

**March 2014**  
Annual criteria review and reference update.

**June 2015**  
Annual editorial review and reference update

**December 2015**  
Annual review  
Removed Chronic myelogenous leukemia (CML) diagnosis per PMPC

**March 2016**  
Annual review and reference update  
Policy number change from 5.04.07 to 5.21.07

**June 2016**  
Annual review and reference update

**June 2017**  
Annual review and reference update

**June 2018**  
Annual editorial review and reference update.  
Removal of multiple myeloma from criteria  
Addition of Cutaneous T-Cell Lymphoma (Mycosis Fungoides and Sezary Syndrome)

**March 2019**  
Annual review and reference update

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**Keywords**

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This policy was approved by the FEP® Pharmacy and Medical Policy Committee on March 15, 2019 and is effective on April 1, 2019.