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).

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, Alferon N, Imlygic, Keytruda, Mekinist, Opdivo, Pegasys, Peginteron, Sylatron, Tafinlar, Yervoy, Zelboraf

**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** for patients with a confirmed diagnosis of hairy cell leukemia, malignant melanoma, multiple melanoma, carcinoid tumor, polycythemia vera, follicular lymphoma, condylomata acuminata, renal cell carcinoma, or AIDS-related Kaposi’s sarcoma.

Intron A may be considered **investigational** 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. Multiple myeloma
8. Polycythemia vera
9. Renal cell cancer

**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
1. Interferon; MedicineNet.com; http://www.medicinenet.com/interferon/article.htm;

Policy History

<table>
<thead>
<tr>
<th>Date</th>
<th>Action</th>
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<tbody>
<tr>
<td>June 2009</td>
<td>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 (2).</td>
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<tr>
<td>July 2009</td>
<td>Criteria updated to remove Roferon, which has been discontinued by manufacturer.</td>
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<tr>
<td>March 2010</td>
<td>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.</td>
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<tr>
<td>March 2010</td>
<td>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</td>
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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.

Carcinoid tumor added to criteria. The National Comprehensive Cancer Network provides detailed practice guidelines for the treatment of individual cancers. The NCCN Drugs and Biologics Compendium recognizes interferon alpha as a treatment for metastatic carcinoid tumors for whom there are no other treatment options. Micromedex also states the evidence for Intron A favors efficacy in the treatment of carcinoid tumors.

Multiple myeloma added to criteria. Micromedex indicates the evidence for Intron A favors efficacy in the treatment of multiple myeloma.

Polycythemia vera added to criteria. The National Cancer Institute currently publishes detailed guidelines for the treatment of individual neoplastic conditions. The NCI guidelines for the treatment of polycythemia vera include interferon-alpha. Micromedex confirms the evidence for Intron A favors efficacy in the treatment of polycythemia vera.

Renal cell cancer added to criteria. Intron A has been used off-label for renal cell cancer for the past three decades, and there are many phase II and III studies. It is not used as much now because of the availability of newer drugs but it is medically necessary to employ it after other options had been exhausted. Interferon alfa is indicated in AHFS Drug Information 2011 for metastatic renal cell carcinoma. In addition, it is designated as an orphan drug by the FDA as treatment for this cancer. Micromedex also confirms the evidence for Intron A favors efficacy in the treatment of renal cell cancer.

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.

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 editorial review review  Removed Chronic myelogenous leukemia (CML) diagnosis per PMPC
March 2016  Annual review and reference update  Policy number change from 5.04.07

**Keywords**

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*This policy was approved by the FEP® Pharmacy and Medical Policy Committee on March 18, 2016 and is effective on April 1, 2016.*

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