BlueCross BlueShield
Federal Employee Program
Federal Employee Program®
750 9th St NW
Washington, D.C. 20001
202.942.1000
Fax 202.942.1125

5.21.007

Section:	Prescription Drugs	**Effective Date:**	July 1, 2024
Subsection:	Antineoplastic Agents	**Original Policy Date:**	December 29, 2011
Subject:	Intron A	**Page:**	1 of 6

Last Review Date: June 13, 2024

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, Besremi, Sylatron

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** if the conditions indicated below are met.

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. 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

Same as above

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 drug monograph; Drug facts. MedicineNet.com.
2. Intron A [package insert]. Rahway, NJ: Merck Sharp & Dohme Corporation; March 2023.
3. NCCN Clinical Practice Guidelines in Oncology® Neuroendocrine and Adrenal tumors (Version 1.2023). National Comprehensive Cancer Network, Inc. August 2023. Accessed on May 2, 2024.
4. NCCN Clinical Practice Guidelines in Oncology® Myeloproliferative Neoplasms (Version 1.2024). National Comprehensive Cancer Network, Inc. December 2023. Accessed on May 2, 2024.
5. NCCN Clinical Practice Guidelines in Oncology® T-Cell Lymphomas (Version 3.2024). National Comprehensive Cancer Network, Inc. April 2024. Accessed on May 2, 2024.
6. NCCN Clinical Practice Guidelines in Oncology® Kidney Cancer (Version 3.2024). National Comprehensive Cancer Network, Inc. March 2024. Accessed on May 2, 2024.
7. NCCN Drugs and Biologics Compendium®. No Longer Recommended Uses. Accessed on May 2, 2024.

Policy History

Date	Action
October 2004	Criteria updated to reflect current guidelines: NIH Consensus Statement on Management of Hepatitis C: 2002 NIH Consensus Statements and State-of-the-Science Statements Volume 19, Number 3, June 10-12, 2002 National Institutes of Health, Office of the Director Diagnosis, Management, and Treatment of Hepatitis C American Association for the Study of Liver Diseases Hepatology, April 2004
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.
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
June 2020	Annual review and reference update
June 2021	Annual review and reference update
March 2022	Annual review and reference update
June 2023	Annual review and reference update. Changed policy number to 5.21.007
June 2024	Annual review and reference update

Keywords

This policy was approved by the FEP® Pharmacy and Medical Policy Committee on June 13, 2024 and is effective on July 1, 2024.