POLICY NUMBER UM ONC_1214	SUBJECT Intron-A™ (interferon alfa-2b)		DEPT/PROGRAM UM Dept	PAGE 1 OF 5
DATES COMMITTEE REVIEWED 09/12/12, 02/14/14, 12/17/15, 08/10/17, 09/13/17, 08/08/18, 07/10/19, 12/11/19	APPROVAL DATE December 11, 2019	EFFECTIVE DATE December 11, 2019	COMMITTEE APPROVAL DATES (latest version listed last) 09/12/12, 02/14/14, 12/17/15, 08/10/17, 09/13/17, 08/08/18, 07/10/19, 12/11/19	
PRIMARY BUSINESS OWNER: UM APPROVED BY: Dr. Andrew Hertler		COMMITTEE/BOARD APPROVAL Utilization Management Committee		
URAC STANDARDS HUM 1	NCQA STANDARDS UM 2		ADDITIONAL AREAS OF IMPACT	
CMS REQUIREMENTS	STATE/FEDERAL REQUIREMENTS		APPLICABLE LINES OF BUSINESS All	

I. PURPOSE

To define and describe the accepted indications for Intron-A (interferon alfa-2b) usage in the treatment of cancer

II. DEFINITIONS

Intron-A (interferon alfa-2b): The antineoplastic activity of interferons may result from a direct antiproliferative effect on the tumor cell and/or the ability of IFN to induce a host response to the tumor (e.g., immunomodulatory effects). Alpha IFNs exert a cytostatic effect on tumor cells, slowing the rate of cell proliferation until cell survival is threatened. The mechanism(s) of antiproliferative activity has not been fully elucidated; several effects may be involved, including the ability of interferons to enhance or inhibit the synthesis of specific proteins, modify cell surface antigen expression, and/or modulate the immune system. Interferon has been shown to prolong all phases of the cell cycle and induce cellular differentiation by promoting cells to enter the nonproliferative G_0 (resting) phase. This differentiation effect is thought to be a key mechanism in the treatment of hairy cell leukemia. Inhibition of tumor cell proliferation may also be related to decreased transcription and expression of several oncogenes. Immunomodulatory effects that may contribute to the antitumor activity of interferons include activation of cytotoxic T cells and/or activation of natural killer (NK) cells. Natural killer cells are lymphocytes that recognize cell surface antigens and lyse certain types of tumor cells. The cytotoxic activity of NK cells against tumor cells can be increased following exposure to interferon, although this effect is highly variable. Interferons may increase the proportion of NK cells that become cytotoxic and/or decrease the time needed for NK cells to reach their maximum cytotoxic effect. In addition, interferons activate macrophages and monocytes, resulting in increased phagocytic activity and enhanced cytotoxicity against tumor cells and other target cells. Alpha interferons have been shown to stimulate production of cytokines such as interleukin (IL)-1beta and IL-1ra (an IL-1 receptor antagonist); thus, alpha-IFNs may affect the inflammatory response.

Intron-A (interferon alfa-2b) is FDA approved for the treatment of patients with:

- AIDS-related Kaposi's sarcoma
- Condyloma acuminatum
- Follicular lymphoma
- Hairy cell leukemia
- Malignant melanoma

Non-FDA approved indications for Oncology include:

- Renal cell carcinoma

Intron-A is available in:

- Injection Powder for Solution: 10 Million IU, 18 Million IU, 50 Million IU
- Injection Solution (multidose vial): 18 Million IU, 25 Million IU
- Injection Solution (in multidose pens): 18 Million IU, 30 Million IU, 60 Million IU

III. POLICY

New Century is responsible for processing all medication requests from network ordering providers. Medications not authorized by New Century may be deemed as not approvable and therefore not reimbursable. Treatment request outside the approved FDA manufacturer labeling or CMS approved compendia must follow CMS Medicare Benefit Policy Manual Chapter 15. If references are not produced, delays may occur to the processing of such request.

Inclusion Criteria: Intron-A (interferon alfa-2b) may be considered medically necessary when any of the following selection criteria is met:

1. **AIDS-Related Kaposi's Sarcoma**
    a. Subsequent systemic therapy given with antiretroviral therapy (ART) for relapsed/refractory advanced, cutaneous, oral, visceral, or nodal disease that has progressed on or not responded to first-line systemic therapy and progressed on alternate first-line systemic therapy.
2. **Hairy Cell Leukemia**
    a. The adult member has a diagnosis of Hairy cell Leukemia.
3. **Renal Cell Carcinoma**
    a. In combination with bevacizumab as first-line therapy for members with relapsed or medically unresectable stage IV disease predominant clear cell histology.
4. **Non-Hodgkin Lymphoma (NHL)**
    a. Used in combination with zidovudine for chronic, smoldering, or acute T-Cell Lymphoma as one of the following
        i. First line therapy
        ii. Additional therapy following complete response on first line therapy
        iii. Additional therapy for acute disease in non-responders if not previously received. **OR**
    b. Second line therapy in combination with arsenic trioxide for non-responders to first-line therapy or as subsequent therapy after high dose therapy/autologous stem cell rescue (HDT/ASCR) for T-Cell lymphoma **OR**
    c. As initial treatment for aggressive follicular NHL in conjunction with an anthracycline-containing combination chemotherapy regimen (i.e. CHOP) OR non-anthracycline containing regimen (i.e. CVP) **OR**

d. As a single-agent therapy in patients with hairy cell leukemia for treatment of refractory or relapse disease within one year of complete response.

5. **Melanoma**

a. Adjuvant treatment as a single agent in adult members for stage III disease with nodal metastases, or for nodal recurrence OR

Exclusion Criteria: Intron-A (interferon alfa-2b) is not considered medically necessary when any of the following selection criteria is met:

1. Intron-A (interferon alfa-2b) is not indicated in any of the following:

b. Concurrent use with another interferon alfa-2b (i.e. Sylatron, PegIntron)

2. Dosing exceeds single dose limit of Intron-A (interferon alfa-2b) 35 MIU/m^2.
3. Indications not supported by CMS recognized compendia or acceptable peer reviewed literature may be deemed as not approvable and therefore not reimbursable.

IV. PROCEDURE

Requests for Intron-A (interferon alfa-2b) shall be reviewed for appropriateness per FDA approved product labeling, the National Comprehensive Cancer Network (NCCN) and American Society of Clinical Oncology (ASCO) clinical guidelines, or CMS approved compendia.

1. **Dosage and Administration**

a. **AIDS-related Kaposi's sarcoma**: 30 million international units/m^2 IM/SUBQ 3 times/wk until disease progression or maximal response is achieved after 16 weeks

b. **Renal Cell Carcinoma:** Doses range from 3 million IU administered SC/IM five times per week up to 36 million IU SC or IM three times per week

c. **Follicular lymphoma**, Initial treatment in conjunction with anthracycline-containing combination chemotherapy: 5 million international units SUBQ 3 times/wk for up to 18 months

d. **Hairy cell leukemia**: 2 million international units/m^2 IM/SUBQ 3 times/wk for up to 6 months

e. **Malignant melanoma, Adjuvant to surgical therapy for high-risk members:** induction, 20 million international units/m^2 IV 5 consecutive days/week for 4 weeks; maintenance, 10 million international units/m^2 SUBQ 3 times/week for 48 weeks

2. **Dosage Adjustments:**

a. Hepatic: (follicular lymphoma) permanently discontinue therapy if SGOT exceeds 5 times the upper limit of normal

b. Hematologic: (follicular lymphoma) delay chemotherapy if neutrophil count less than 1500/mm^3 or platelet count less than 75,000/mm^3

c. Hematologic: (follicular lymphoma) withhold therapy for neutrophil count less than 1000/mm^3 or platelet count less than 50,000 mm^3; reduce dose by 50% for neutrophil count

greater than 1000/mm^3 but less than 1500/mm^3; increase to starting dose with neutrophil count greater than 1500/mm^3

d. Renal: (follicular lymphoma) permanently discontinue therapy if serum creatinine greater than 2 mg/dL

e. Hepatic: (malignant melanoma) withhold therapy if SGPT/SGOT greater than 5 to 10 times upper limit of normal; once resolved, restart therapy at 50% of previous dose; permanently discontinue if SGPT/SGOT greater than 10 times upper limit of normal

f. Hematologic: (malignant melanoma) withhold therapy if granulocyte count greater than 250/mm^3 but less than 500/mm^3; once resolved, restart therapy at 50% of previous dose; permanently discontinue if granulocyte count less than 250/mm^3

g. Hematologic: (chronic hepatitis B) WBC count less than 1.5 x 10^9/L; granulocyte count less than 0.75 x 10^9/L; platelet count less than 50 x 10^9 /L) reduce dose 50%

h. Hematologic: (chronic hepatitis B) WBC count less than 1 x 10^9/L; granulocyte count less than 0.5 x 10^9/L; platelet count less than 25 x 10^9/L) permanently discontinue treatment

i. Severe adverse reactions: (hairy cell leukemia, AIDS-related Kaposi's sarcoma, chronic hepatitis B, and chronic hepatitis C members) reduce dose by 50% or temporarily discontinue therapy if severe adverse reactions develop; once adverse reactions resolve, resume treatment at 50% of normal dose; discontinue permanently if severe reactions persist or recur

j. Severe adverse reactions: (malignant melanoma) temporarily discontinue therapy if severe adverse reactions develop; once adverse reactions resolve, resume treatment at 50% of normal dose; discontinue permanently if severe reactions persist or recur

3. **Monitoring**

a. Hairy cell leukemia: improvement in blood counts may indicate efficacy

b. Malignant melanoma, follicular lymphoma, AIDS-related Kaposi's sarcoma: objective evidence of tumor response may be indicative of efficacy

c. Malignant melanoma: CBC with differential and hepatic function; weekly during induction, then monthly

d. CBC with differential, including hemoglobin and platelets; baseline and periodically

e. Drug screening; consider periodically in members with a history of psychiatric conditions or substance abuse

f. Electrolyte panel; baseline and periodically

g. Liver function tests, baseline and periodically

h. TSH; baseline and periodically

i. Chest X-ray; baseline, then periodically if clinically indicated

j. ECG; baseline and during therapy in members with preexisting cardiac abnormalities or advanced-stage cancer

k. Ophthalmologic exam; baseline in all members, and during therapy in members with preexisting ophthalmologic disorders

l. Psychiatric symptoms; in members with a history of psychiatric conditions or substance abuse

V. APPROVAL AUTHORITY

1. Review – UM Department
2. Final Approval – UM Committee

VI. ATTACHMENTS

None

VII. REFERENCES

1. Intron-A prescribing information**.** Schering Corporation, Merck & Co. Whitehouse Station, NJ. 2018.
2. Clinical Pharmacology Elsevier Gold Standard. 2019.
3. Micromedex® Healthcare Series: Thomson Micromedex, Greenwood Village, Co. 2019.
4. National Comprehensive Cancer Network. Cancer Guidelines and Drugs and Biologics Compendium. 2019.
5. AHFS Drug Information. American Society of Health-Systems Pharmacists or Wolters Kluwer Lexi-Drugs. Bethesda, MD. 2019.