INTERFERON (IFN) THERAPY
RX502.006

COVERAGE:

Coverage allowed statements for each class of interferons, ALPHA (alfa), BETA, and GAMMA, are discussed separately.

**********************************************************************

RECOMBINANT OR NATURAL INTERFERON ALFA (Alfa 2-A, Alfa 2-B, and Alfa N-3):

1. IFN2-A, IFN Alfa 2a, rIFN-A, or IFLrA (Roferon-A) may be eligible for coverage for the following indications:

   • Hairy cell leukemia,
   • AIDS-related Kaposi’s sarcoma,
   • Chronic myelogenous leukemia (CML) – (as a first line treatment of patients with Philadelphia chromosome-positive CML in first chronic phase),
   • Multiple myeloma (MM) – (as a component of first-line treatment for patients with MM, or as maintenance therapy for patients with MM that have responded to first-line therapy), and
   • Non-Hodgkin's lymphoma (NHL) – (combined with cytotoxic agents as first-line therapy of aggressive low-grade (follicular) or intermediate-grade NHL);

2. IFN 2-B, IFN Alfa 2b, IFN-alpha 2, rIFN-2a, or a-2-interferon (Intron A) may be eligible for coverage for the following indications:

   • Hairy cell leukemia - (patients either splenectomized and non-splenectomized),
   • Primary or recurrent malignant melanoma (MM) – (as an adjunct to surgical treatment for patients with malignant melanoma who are free of disease but at high risk for systemic recurrence within 56 days of surgery),
   • Condylomata acuminata – (for intralesional treatment of genital or venereal warts in patients who do not respond to other treatment modalities or whose lesions are more readily treatable by IFN 2-B),
   • AIDS-related Kaposi’s sarcoma,
   • Chronic hepatitis NANB/C – (patients with compensated liver disease and a history of blood or blood product exposure or who are ACV antibody positive. Coverage may be considered when using IFN alfa with or without ribavirin as an initial treatment of hepatitis C, or as a salvage treatment of relapsed hepatitis C), and
   • Chronic hepatitis B – (patients with compensated liver disease and hepatitis B virus (HBV) replication. NOTE: patients must be serum HBEAG positive for at least 6 months and have HBV
replication [serum HBEAG positive] with elevated serum ALT); and,

3. IFN N-3 or IFN Alfa n3 (Alferon N) **may be eligible for coverage** for the following indication:

   - Condylomata acuminata - (for intralesional treatment of genital or venereal warts).

Recombinant or natural IFN alfa is considered **investigational** for the treatment of any off-label hematologic malignancy other than those previously listed and **coverage is not allowed**.

******************************************************************************
INTERFERON BETA (Beta 1-A and Beta 1-B):
******************************************************************************

1. IFN Beta 1-A (Avonex) **may be eligible for coverage** for the following indication:

   - Multiple Sclerosis (MS) - (for relapsing forms of MS to slow the accumulation physical disability and decrease the frequency of clinical exacerbations); and,

2. IFN Beta 1-B (Betaseron) **may be eligible for coverage** for the following indication:

   - Multiple Sclerosis (MS) - (for ambulatory patients with relapsing-remitting MS to reduce the frequency of clinical exacerbations).

Recombinant or natural IFN beta is considered **investigational** for the treatment of any indication(s) other than the one previously listed and **coverage is not allowed**.

******************************************************************************
INTERFERON GAMMA (Gamma 1-B):
******************************************************************************

1. IFN Gamma 1-B (Actimmune) **may be eligible for coverage** for the following indications:

   - Chronic granulomatous disease - (in reducing the frequency and severity of serious infections associated with this disease).

Recombinant or natural IFN gamma is considered **investigational** for the treatment of any indication(s) other than the one previously listed and **coverage is not allowed**.

******************************************************************************
Recombinant and human leukocyte-derived IFNs for the treatment of any off-label solid tumor indications are **not eligible for coverage** as they are considered **investigational**. These indications include, but are not limited to, the following:

   - Bladder cancer,
   - Breast cancer,
   - Cancer or precancers of oral cavity,
   - Carcinoid tumor or carcinoid syndromes,
• Cervical intraepithelial neoplasia II associated with human papillomavirus infection,
• Colorectal cancer,
• Cutaneous squamous cell cancer (including actinic keratoses, basal cell carcinoma),
• Malignant brain tumors,
• Malignant islet-cell tumors,
• Mature-growing testicular teratoma,
• Medullary thyroid carcinoma,
• Melanoma,
• Merkel cell tumor,
• Metastatic amine precursor uptake decarboxylase cell tumors (apudomas),
• Neuroendocrine tumors,
• Non-small-cell lung cancer,
• Osteosarcoma,
• Ovarian cancer,
• Pancreatic cancer,
• Recurrent or metastatic head and neck cancers,
• Recurrent respiratory papillomatosis,
• Relapsed adult nephroblastoma, and
• Renal cell carcinoma.

DESCRIPTION:

**Interferons (IFNs)** comprise approximately 20 naturally occurring proteins produced by cells in response to foreign components, such as microbes, tumors, and antigens. These naturally occurring IFNs apply protection on other cells, preventing them from becoming infected. Their name comes from their ability to "interfere" with a subsequent viral attack of target cells.

Three classes of IFNs have been identified: **ALPHA**, **BETA**, and **GAMMA**. Each class is chemically unique, synthesized and release primarily by different sets of cells, and has a specific function.

IFNs play an important role in the immune system. IFNs may profoundly affect other vital cellular and body functions, including; metabolism, cell proliferation, hormone stimulation, immunity, and tumor development. This can induce the complex actions of IFN, which are not completely understood. These complex actions are:

• Antiviral,
• Antimicrobial,
• Antitumor,
• Antiproliferative,
• Antiangiogenic,
• Immunomodulatory, and
• Gene regulatory effects.

**FDA Approval Dates:**
- IFN Alfa 2-A (Roferon-A) in 1986
- IFN Beta 1-A (Avonex) on May 17, 1996
- IFN Beta 1-B (Betaseron) on July 23, 1993

RATIONALE:
There are two rationales for the use of IFNs in clinical oncology.

First, there is evidence to suggest that IFNs have a direct antiproliferative effect on some cancer cells by:

- increasing the length of the cell,
- depleting essential intracellular metabolites, and
- enhancing cell lysis.

Second, IFNs may have indirect effects, such as:

- enhancement of cell-surface antigen expression,
- enhancement of macrophage and lymphocyte cytotoxicity, and
- induction of antibodies to tumor cells.

When used for treatment of non-oncological indications the evidence suggests IFNs have antiviral and immunomodulatory activity. This combination improves the ability of the immune system to control and eliminate the viral load.

DISCLAIMER:

State and federal law, as well as contract language, including definitions and specific inclusions/exclusions, takes precedence over Medical Policy and must be considered first in determining coverage. The member’s contract benefits in effect on the date that services are rendered must be used. Any benefits are subject to the payment of premiums for the date on which services are rendered. Medical technology is constantly evolving, and we reserve the right to review and update Medical Policy periodically. HMO Blue Texas physicians who are contracted/affiliated with a capitated IPA/medical group must contact the IPA/medical group for information regarding HMO claims/reimbursement information and other general polices and procedures.

Blue Cross and Blue Shield of Texas, a Division of Health Care Service Corporation, a Mutual Legal Reserve Company
Southwest Texas HMO, Inc.* d/b/a HMO Blue® Texas
* Independent Licensees of the Blue Cross and Blue Shield Association

Posted Jan. 7, 2003