



CIGNA MEDICAL COVERAGE POLICY

The following Coverage Policy applies to all health benefit plans administered by CIGNA Companies including plans formerly administered by Great-West Healthcare, which is now a part of CIGNA.

**Subject Interferon Gamma-1b
(Actimmune™)**

Effective Date 7/15/2011
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Coverage Policy Number 5014

Table of Contents

Coverage Policy	1
General Background	2
Coding/Billing Information	2
References	3
Policy History.....	4

Hyperlink to Related Coverage Policies

INSTRUCTIONS FOR USE

Coverage Policies are intended to provide guidance in interpreting certain **standard** CIGNA HealthCare benefit plans. Please note, the terms of a customer's particular benefit plan document [Group Service Agreement (GSA), Evidence of Coverage, Certificate of Coverage, Summary Plan Description (SPD) or similar plan document] may differ significantly from the standard benefit plans upon which these Coverage Policies are based. For example, a customer's benefit plan document may contain a specific exclusion related to a topic addressed in a Coverage Policy. In the event of a conflict, a customer's benefit plan document **always supercedes** the information in the Coverage Policies. In the absence of a controlling federal or state coverage mandate, benefits are ultimately determined by the terms of the applicable benefit plan document. Coverage determinations in each specific instance require consideration of 1) the terms of the applicable benefit plan document in effect on the date of service; 2) any applicable laws/regulations; 3) any relevant collateral source materials including Coverage Policies and; 4) the specific facts of the particular situation. Coverage Policies relate exclusively to the administration of health benefit plans. Coverage Policies are not recommendations for treatment and should never be used as treatment guidelines. In certain markets, delegated vendor guidelines may be used to support medical necessity and other coverage determinations. Proprietary information of CIGNA. Copyright ©2011 CIGNA

Coverage Policy

CIGNA covers Interferon Gamma 1-b (Actimmune™) as medically necessary for EITHER of the following indications:

- reduction of the frequency and severity of serious infections associated with chronic granulomatous disease (CGD)
- delaying time to disease progression in individuals with severe, malignant osteopetrosis

The dosage, frequency, site of administration, and duration of therapy are reasonable, clinically appropriate, and supported by evidence-based literature and adjusted based upon severity, alternative available treatments, and previous response to interferon gamma 1-b (Actimmune™) therapy.

FDA Approved Indications

Actimmune is indicated for reducing the frequency and severity of serious infections associated with chronic granulomatous disease (CGD). Actimmune is indicated for delaying time to disease progression in patients with severe, malignant osteopetrosis.

FDA Recommended Dosing

For CGD and severe, malignant osteopetrosis, it is recommended to give interferon gamma-1b three times weekly (e.g., Monday, Wednesday, and Friday). For patients with body surface area exceeding 0.5 m², the recommended dosage is 50 mcg/m² three times weekly. However, those with body surface area of 0.5 m² or lower should receive a dosage of 1.5 mcg/kg three times weekly (i.e., based on body weight, not surface area). Although safety and efficacy have not been established in this age group, children one month of age or older with osteopetrosis have received interferon gamma-1b in a dosage of 1.5 mcg/kg three times weekly.

Drug Availability

Actimmune is available in single use vials for subcutaneous injection containing 100mcg interferon gamma-1B.

General Background

Pharmacology/Disease Overview

Interferon-gamma binds to a cell surface receptor classified as Type 2 interferon. Specific effects of interferon-gamma include the enhancement of the oxidative metabolism of macrophages, antibody-dependent cellular cytotoxicity (ADCC), activation of natural killer (NK) cells, and the expression of Fc (crystallizable fragments) receptors and major histocompatibility antigens. Actimmune is a synthesized version of interferon gamma-1b, a naturally-occurring biologic response modifier. It is indicated to reduce the frequency and severity of infections in patients with CGD and to delay the progression of severe, malignant osteopetrosis.

The pharmacokinetics of interferon gamma-1b 100 mcg/m² have been investigated in 24 healthy male subjects given intravenously (IV), intramuscularly (IM) and subcutaneously (SQ). Interferon gamma-1b is rapidly cleared after intravenous administration (1.4 L/min). It is slowly absorbed (>89%) after intramuscular and subcutaneous injection. The mean elimination half-life after intravenous administration was 38 minutes, for IM and SQ dosing were 2.9 and 5.9 hours, respectively, with no evidence of accumulation following subcutaneous administration of 100 mcg/m² once daily for 12 days. Peak plasma concentrations occurred four hours (1.5 ng/ml) after IM dosing and seven hours (0.6 ng/ml) after SQ dosing. Pharmacokinetics of interferon gamma-1b has not been evaluated in females, pediatric patients, geriatric patients, or patients with renal or hepatic insufficiency.

Clinical Efficacy

A randomized, double-blind, placebo-controlled phase III trial (INSPIRE [International Study of Survival Outcomes in IPF with Interferon Gamma-1b] clinical trial) evaluated Actimmune (interferon gamma-1b) for idiopathic pulmonary fibrosis (IPF) in 600 patients with mild-to-moderate lung function impairment. The primary endpoint of the trial was survival. Subjects were randomized 2:1 to receive either Actimmune 200 micrograms three times a week or placebo. On March 5, 2007, the Food and Drug Administration (FDA) notified healthcare professionals of the early termination of the INSPIRE clinical study of interferon gamma-1b for IPF. The study was stopped because an interim analysis showed that patients with IPF who received interferon gamma-1b did not benefit. An analysis showed that 14.5% of patients treated with interferon gamma-1b died as compared to 12.7% of patients treated with placebo. Interferon gamma-1b is not approved by the FDA to treat IPF.

Adverse Reactions

The most frequent adverse effects reported with interferon gamma-1b are flu-like symptoms (e.g., fever, headache, chills, myalgia, and fatigue) and erythema or tenderness at the injection site. These adverse effects usually are mild, and only rarely necessitate discontinuance of the drug. Caution should be exercised when using interferon gamma-1b with other myelosuppressive agents. Contraindications for interferon gamma-1b are in patients who develop or have known hypersensitivity to interferon gamma, E. Coli-derived products, or any component of the product. Isolated cases of acute serious hypersensitivity reactions have been observed in patients receiving interferon gamma-1b.

Coding/Billing Information

Note: This section is not in use.

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Policy History

Pre-Merger Organizations	Last Review Date	Policy Number	Title
CIGNA HealthCare Great-West Healthcare	7/15/2008	5014	Interferon Gamma-1b (Actimmune™)

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