BlueCross BlueShield Arizona

An Independent Licensee of the Blue Cross Blue Shield Association

PHARMACY COVERAGE GUIDELINE

ACTIMMUNE® (interferon gamma-1b) Generic Equivalent (if available)

This Pharmacy Coverage Guideline (PCG):
- Provides information about the reasons, basis, and information sources we use for coverage decisions
- Is not an opinion that a drug (collectively "Service") is clinically appropriate or inappropriate for a patient
- Is not a substitute for a provider's judgment (Provider and patient are responsible for all decisions about appropriateness of care)
- Is subject to all provisions e.g. (benefit coverage, limits, and exclusions) in the member's benefit plan; and
- Is subject to change as new information becomes available.

Scope
- This PCG applies to Commercial and/or Marketplace plans
- This PCG does not apply to the Federal Employee Program, Medicare Advantage, Medicaid or members of out-of-state Blue Cross and/or Blue Shield Plans

Instructions & Guidance
- To determine whether a member is eligible for the Service, read the entire PCG.
- This PCG is used for FDA approved indications including, but not limited to, a diagnosis and/or treatment with dosing, frequency, and duration.
- Use of a drug outside the FDA approved guidelines, refer to the appropriate Off-Label Use policy.
- The "Criteria" section outlines the factors and information we use to decide if the Service is medically necessary as defined in the Member's benefit plan.
- The "Description" section describes the Service.
- The "Definition" section defines certain words, terms or items within the policy and may include tables and charts.
- The "Resources" section lists the information and materials we considered in developing this PCG
- **We do not accept patient use of samples as evidence of an initial course of treatment, justification for continuation of therapy, or evidence of adequate trial and failure.**
- Information about medications that require prior authorization is available at www.azblue.com/pharmacy. You must fully complete the request form and provide chart notes, lab workup and any other supporting documentation. The prescribing provider must sign the form. Fax the form to BCBSAZ Pharmacy Management at (602) 864-3126 or email it to Pharmacyprecert@azblue.com.

Medical Necessity Requirements for ACTIMMUNE (interferon gamma 1b)

Criteria for Initial Therapy:

Prescriber Qualifications
- Prescribed by a physician specializing in the diagnosis or in consultation with an endocrinologist or immunologist depending on the indication

Indication
- Chronic Granulomatous Disease (CGD) to reduce frequency and severity of serious infections
- Severe malignant osteopetrosis (SMO) to delay time to disease progression

ORIGINAL EFFECTIVE DATE: 02/20/2025 | ARCHIVE DATE: | LAST REVIEW DATE: 02/19/2026 | LAST CRITERIA REVISION DATE: 02/19/2026

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Age Requirement
- 1 year or older for Chronic Granulomatous Disease
- 1 month or older for Severe malignant osteopetrosis

Baseline Clinical Evaluation
- Chronic Granulomatous Disease (CGD)
  - Molecular genetic test identifying a gene related mutation linked to CGD
  - Receiving standard of care antimicrobial prophylaxis (bacterial and fungal)
- Severe malignant osteopetrosis (SMO) **BOTH** of the following:
  - Radiographic imaging demonstrating skeletal features related to osteopetrosis
  - Molecular genetic test identifying a gene related mutation linked to SMO
- Complete blood count with differential
- Renal function test
- Liver function test
- Urinalysis

Brand Specific Criteria
- Have failure, contraindication, or intolerance with three generic equivalents (if available) for at least three months each. **Note**: Any failure, contraindication, or intolerance to the generic drugs should be reported to the FDA (see Definitions section)

Safety
- **NO** FDA labeled contraindications such as:
  - Known hypersensitivity to interferon gamma
  - Hypersensitivity to Escherichia coli (E. coli) derived products
  - Hypersensitivity to any component of the product
- Does not have a latex allergy (glass vial contains natural rubber stopper)

Documentation Requirements
- A completed request form must be submitted including:
  - Chart notes
  - Lab results (molecular genetic test results, radiographic imaging reports)
  - Supporting clinical documentation

Initial Therapy Criteria Approval Duration
- 6 months OR end of plan year

Criteria for Continuation of Therapy (renewal therapy):

Note: Manufacturer assistance (e.g., coupons, samples, etc.) are not considered for continuation of therapy.

Prescriber Qualification
- Continues to be seen by a physician specializing in or is in consultation with an endocrinologist or immunologist depending on the indication

Clinical Response

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- Chronic Granulomatous Disease (CGD):
  - Reduced frequency and severity of infections
  - No hypersensitivity to Escherichia coli (E. coli) derived products
  - No hypersensitivity to any component of the product
- Severe malignant osteopetrosis (SMO):
  - Hematologic recovery (improvement in platelets and hemoglobin)
  - Increase in leukocyte superoxide activity
  - Decrease in trabecular bone volume

Adherence

- Adherence to the prescribed therapy regimen has been documented

Brand Specific Criteria

- Have failure, contraindication, or intolerance with three generic equivalents (if available) for at least three months each. **Note**: Any failure, contraindication, or intolerance to the generic drugs should be reported to the FDA (see Definitions section

Safety

- No development of contraindications or significant adverse drug effects such as:
  - Hypersensitivity to interferon gamma
  - Hypersensitivity to Escherichia coli (E. coli) derived products
  - Hypersensitivity to any component of the product
  - Neutropenia
  - Thrombocytopenia
  - Decreased mental status, gait disturbances, dizziness

Documentation Requirements

- Chart notes
- Supporting clinical documentation with evidence of improvement in given indication
- Lab values that confirm safe use (e.g., hematologic recovery, leukocyte activity, bone volume changes)

Continuation Therapy Criteria Approval Duration

- 12 months OR end of plan year

Criteria for Off-Label Use Requests:

Criteria for a request for non-FDA use or indication, treatment with dosing, frequency, or duration outside the FDA-approved dosing, frequency, and duration, refer to one of the following Pharmacy Coverage Guideline:

1. Off-Label Use of Non-Cancer Medications

2. Off-Label Use of Cancer Medications

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Benefit Type:

Pharmacy Benefit:
ACTIMMUNE

Medical Benefit:
ACTIMMUNE

Coding:

HCPCS: J9216

Description:

Actimmune (interferon gamma-1b) is an interferon gamma indicated for: reducing the frequency and severity of serious infections associated with Chronic Granulomatous Disease (CGD) and delaying time to disease progression in patients with severe, malignant osteopetrosis (SMO).

Chronic granulomatous disease (CGD) is a genetically diverse disorder marked by recurrent, severe bacterial and fungal infections as well as granuloma development. CGD can cause growth failure, poor wound healing, diarrhea, and granulomatous dermatitis. Physical exam may reveal enlarged liver or spleen, or lymphadenitis. Individuals with CGD can develop life-threatening infections at any time, even after long periods without infection. The majority of cases of CGD are identified prior to five years of age. Key aspects of CGD management include antimicrobial and immunomodulatory prophylaxis, prompt identification of infections, and aggressive treatment of infectious complications. Individuals with CGD are managed with lifelong prophylactic antibacterial and antifungal therapy, with or without additional immunomodulatory treatment.

Osteopetrosis is a group of rare bone disorders marked by poor osteoclast function, causing high bone density. Despite high bone density, the bones are more brittle and fracture risk increases. Bone growth into marrow spaces or cranial nerve openings can disrupt blood cell production and nervous system function. Disorders of hematopoiesis may manifest as profound anemia, heightened bleeding tendencies, recurrent infections, and hepatosplenomegaly. Cranial nerve involvement may lead to deficits such as vision impairment, hearing impairment, or various cranial nerve palsies. Osteopetrosis is classified according to clinical severity and mode of inheritance into three forms: a malignant autosomal recessive infantile type, a benign adult autosomal dominant type (which may, in some cases, present with significant severity), and an intermediate form. Hematopoietic Stem Cell Transplantation (HSCT) is the main treatment. Supportive options are calcium, phosphate, vitamin D, corticosteroids, erythropoietin for anemia, and gamma interferon to boost immunity and bone resorption.

Definitions:

U.S. Food and Drug Administration (FDA) MedWatch Forms for FDA Safety Reporting
MedWatch Forms for FDA Safety Reporting | FDA

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Genetic Mutations of Chronic Granulomatous Disease: *CYBA, CYBB, NCF1, NCF2, NCF4*
Genetic Mutations of osteopetrosis: *CAII, CLCN7, IKBLG, ITGB3, LRP5, OSTM1, PLEKHM1, SNX10, TCIRG1, TNFSF11, and TNFRSF11A*

Resources:

Actimmune (interferon gamma-1b) injection, solution prescribing information, revised by Horizon Therapeutics USA, Inc. 12-2024 at DailyMed, http://dailymed.nlm.nih.gov. Accessed October 29, 2025.

Manolagas SC. Normal skeletal development and regulation of bone formation and resorption. In: UpToDate, Rosen CJ, Rubinow K (Eds). UpToDate, Waltham, MA.: Available at http://uptodate.com. Literature current through November 2025. Topic last updated October 03, 2025. Accessed December 09, 2025.

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Marciano BE, Zerbe CS, Holland SM. Chronic granulomatous disease: Treatment and prognosis: In: UpToDate, Orange JS, TePas E (Eds). UpToDate, Waltham, MA.: Available at http://uptodate.com. Literature current through November 2025. Topic last updated November 18, 2025. Accessed December 09, 2025.

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Tangye SG, Al-Herz W, Bousfiha A, et al. Human inborn errors of immunity: 2022 update on the classification from the International Union of Immunological Societies Expert Committee. *J Clin Immunol*. 2022; 42:1473-1507. Re-evaluated December 09, 2025.

Wu CC, Econs MJ, DiMeglio LA, et al. Diagnosis and management of osteopetrosis: consensus guidelines from the Osteopetrosis Working Group. *J Clin Endocrinol Metab*. 2017; 103: 311-3123. Re-evaluated December 09, 2025.

Key LL, Rodriguiz RM, Willi SM, et al: Long-Term Treatment of Osteopetrosis with Recombinant Human Interferon Gamma. NEJM 1995 June 15;332 (24):1594-1599 DOI: 10.1056/NEJM199506153322402.