Drug and Biologic Coverage Policy

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Coverage Policy Number IP0201

Interferon Gamma-1b for Non-Oncology Uses

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INSTRUCTIONS FOR USE
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Overview

This policy supports medical necessity review for interferon gamma-1b (**Actimmune®**) for non-oncology indications.

The use of interferon gamma-1b (Actimmune®) for oncology indications is addressed in a separate coverage policy. Please refer to the related coverage policy link above (Oncology Medications).

Receipt of sample product does not satisfy any criteria requirements for coverage.

Medical Necessity Criteria

Interferon gamma-1b (Actimmune) is considered medically necessary when ONE of the following is met (1 or 2):

1. **Chronic Granulomatous Disease.** Individual meets **BOTH** of the following criteria (A and B):

A. Documented diagnosis confirmed by a molecular genetic test identifying variants linked to chronic granulomatous disease (for example, biallelic pathogenic variants in *CYBA, NCF1*, *NCF2,* and *NCF4* cause autosomal recessive CGD; pathogenic variants in *CYBB* cause X-linked CGD)
B. The medication is prescribed by, or in consultation with, a medical geneticist, immunologist, or physician who specializes in chronic granulomatous disease

2. **Severe Malignant Osteopetrosis, Infantile.** Individual meets **BOTH** of the following criteria (A and B):
   A. Documented diagnosis confirmed by **ONE** of the following (i or ii):
      i. Individual has had radiographic (X-ray) imaging demonstrating skeletal features related to osteopetrosis (for example, increased bone density, diffuse and focal sclerosis of varying severity, modelling defects at metaphyses)
      ii. Individual has had a molecular genetic test identifying variants linked to severe, infantile malignant osteopetrosis (for example, biallelic pathogenic variants in *CA2, CLCN7, IKBKG, ITGB3, OSTM1, PLEKHM1, RANKL, RANK, TCIRG1, TNFRSF11A,* or *TNFSF11*)
   B. The medication is prescribed by, or in consultation with, an endocrinologist, geneticist, or physician who specializes in severe malignant osteopetrosis

When coverage is available and medically necessary, the dosage, frequency, duration of therapy, and site of care should be reasonable, clinically appropriate, and supported by evidence-based literature and adjusted based upon severity, alternative available treatments, and previous response to therapy.

Reauthorization Criteria

Interferon gamma-1b (Actimmune) is considered medically necessary for continued use when initial criteria are met AND there is documentation of beneficial response.

Authorization Duration

Initial approval duration: up to 12 months
Reauthorization approval duration: up to 12 months

Conditions Not Covered

Any other use is considered experimental, investigational or unproven.

Background

OVERVIEW
Actimmune, an interferon gamma, is indicated for the following uses:[1]

- **Chronic granulomatous disease** (CGD), to reduce the frequency and severity of serious infections.
- **Severe, malignant osteopetrosis** (SMO), to delay time to disease progression.

In both disorders, the exact mechanism(s) by which Actimmune has a treatment effect has not been established. Changes in superoxide levels during Actimmune therapy do not predict efficacy and should not be used to assess patient response to therapy.

Disease Overview
Chronic Granulomatous Disease (CGD)
CGD, a primary immune deficiency disease, is caused by defects in the nicotinamide adenine dinucleotide phosphate (NAPDH) oxidase (NOX) enzyme.[2,3] This enzyme is needed by phagocytes (a type of white blood cell) to kill certain types of bacteria and fungi. Patients with CGD are at risk of contracting recurrent and sometimes severe bacterial or fungal infections. Patients may need lifelong regimens of antibiotics and

antifungals to prevent infections and use of Actimmune may also help reduce the number of severe infections. Mutations in one of five different genes that encode components of the NADPH (*CYBA, CYBB, NCF1, NCF2*, or *NCF4*) cause CGD. Some patients with CGD do not have an identified mutation in any of these genes and the cause of the condition in these individuals is unknown.

The American Academy of Allergy, Asthma and Immunology and the American College of Allergy, Asthma and Immunology have jointly accepted responsibility for establishing the practice parameter for the diagnosis and management of primary immunodeficiency.[4] The practice parameter (2015) recommends patients with CGD be given antibacterial and antifungal prophylaxis and Actimmune.

Severe, Malignant Osteopetrosis (SMO)
SMO is an inherited disorder characterized by osteoclast defect and deficient phagocyte oxidative metabolism.[1] There is a reduction in osteoclastic bone reabsorption, which results in bone density overgrowth and poor structural integrity (i.e., bones are more brittle and susceptible to fracture).[5,6] In some cases, this is also accompanied by skeletal abnormalities.[5] The cause of SMO is unknown in some patients, however, variants in one of the following genes have been found to be associated with osteopetrosis: *CA2, CLCN7, IKBLG, ITGB3, LRP5, OSTM1, PLEKHM1, SNX10, TCIRG1, TNFRSF11A, TNFSF11*. The Osteopetrosis Working Group developed expert consensus guidelines for the diagnosis and management of osteopetrosis (2017).[7] The guidelines recommend determination of diagnosis by classic radiographic (X-ray) features of osteopetrosis followed up by genetic testing to differentiate between the different forms of osteopetrosis with unique complications. The guidelines suggest the use of Actimmune to be considered experimental in non-infantile osteopetrosis with limited clinical experience. Furthermore, the guidelines acknowledge the FDA indication for SMO and advise that the indication pertains only to severe infantile osteopetrosis.

References

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3. Genetics Home Reference. National Institutes of Health, U.S. National Library of Medicine. Available at https://ghr.nlm.nih.gov/. Accessed on March 29, 2023. Search terms: chronic granulomatous disease.
4. Bonilla F, Khan D, Ballas Z, et al. Practice parameter for the diagnosis and management of primary immunodeficiency. The Journal of Allergy and Clinical Immunology. 2015;136:5:1186-1205.e78.
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6. Genetics Home Reference. National Institutes of Health, U.S. National Library of Medicine. Available at https://ghr.nlm.nih.gov/. Accessed on March 29, 2023. Search terms: osteopetrosis.
7. Wu C, Econs M, DiMeglio L, et al. Diagnosis and management of osteopetrosis: consensus guidelines from the osteopetrosis working group. J Clin Endocrinol Metab. 2017;102:3111-3123.