PRIOR AUTHORIZATION POLICY

POLICY: Interferon – Actimmune Prior Authorization Policy
- Actimmune® (interferon gamma-1b subcutaneous injection – Horizon)

REVIEW DATE: 05/29/2024; selected revision 07/17/2024 and 09/18/2024

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 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.

POLICY STATEMENT

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Prior Authorization is recommended for prescription benefit coverage of Actimmune. Because of the specialized skills required for evaluation and diagnosis of patients treated with Actimmune as well as the monitoring required for adverse events and long-term efficacy, approval requires Actimmune to be prescribed by or in consultation with a physician who specializes in the condition being treated. All approvals are provided for the duration noted below.

Automation: None.

RECOMMENDED AUTHORIZATION CRITERIA

Coverage of Actimmune is recommended in those who meet one of the following criteria:

FDA-Approved Indications

1. **Chronic Granulomatous Disease.** Approve for 1 year if the patient meets BOTH of the following (A and B):
   - **A)** Diagnosis has been established by a molecular genetic test identifying a gene-related pathogenic variant linked to chronic granulomatous disease; AND
     Note: Examples of gene-related pathogenic variants linked to chronic granulomatous disease include biallelic pathogenic variants in *CYBA, CYBB, NCF1, NCF2,* and *NCF4*.
   - **B)** The medication is prescribed by or in consultation with an immunologist, a hematologist, or an infectious disease specialist.

2. **Malignant Osteopetrosis, Severe Infantile.** Approve for 1 year if the patient meets BOTH of the following (A and B):
   - **A)** Diagnosis has been established by ONE of the following (i or ii):
     - **i.** Patient has had radiographic (X-ray) imaging demonstrating skeletal features related to osteopetrosis; OR
     - **ii.** Patient has had a molecular genetic test identifying a gene-related pathogenic variant linked to severe, infantile malignant osteopetrosis; AND
       Note: Examples of gene-related pathogenic variants linked to osteopetrosis include *CA2, CLCN7, IKBLG, ITGB3, LRP5, OSTM1, PLEKHM1, SNX10, TCIRG1, TNFRSF11A,* and *TNFSF11*.
   - **B)** The medication is prescribed by or in consultation with an endocrinologist.

CONDITIONS NOT RECOMMENDED FOR APPROVAL

Coverage of Actimmune is not recommended in the following situations:

1. Coverage is not recommended for circumstances not listed in the Recommended Authorization Criteria. Criteria will be updated as new published data are available.

REFERENCES

1. Actimmune® subcutaneous injection [prescribing information]. Lake Forest, IL: Horizon; May 2021.
2. National Institute of Allergy and Infectious Diseases. Chronic granulomatous disease (CGD). Available at: https://www.niaid.nih.gov/diseases-conditions/chronic-granulomatous-disease-cgd#:~:text=Chronic%20granulomatous%20disease%20(CGD)%20is,threatening%20bacterial%20and%20fungal%20infections. Last reviewed May 20, 2022. Accessed on May 29, 2024.
3. Genetics Home Reference. National Institutes of Health, U.S. National Library of Medicine. Available at https://ghr.nlm.nih.gov/. Accessed on May 29, 2024. Search terms: chronic granulomatous disease.

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4. Bonilla F, Khan D, Ballas Z, et al. Practice parameter for the diagnosis and management of primary immunodeficiency. *The J Allergy Clin Immunol*. 2015;136(5):1186-1205.e78.
5. Charoenngam N, Nasr A, Shirvani A, Holick MF. Hereditary metabolic bone diseases: a review of pathogenesis, diagnosis and management. *Genes*. 2022;13:1880.
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.

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