PRIOR AUTHORIZATION POLICY

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

REVIEW DATE: 04/07/2021

OVERVIEW

Actimmune, an interferon gamma, is indicated for the following uses:[1]
- **Chronic granulomatous disease** (CGD), reducing the frequency and severity of serious infections.
- **Severe, malignant osteopetrosis** (SMO), delaying time to disease progression age.

In both disorders, the exact mechanism(s) of Actimmune's 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 is an inherited primary immunodeficiency caused by functional impairment of the dihydronicotinamide-adenine dinucleotide phosphate (NADPH) oxidase complex in neutrophilic granulocytes and monocytes characterized by recurrent and severe infections, dysregulated inflammation, and autoimmunity.[2] CGD may present any time from infancy to late adulthood; however, the vast majority of affected individuals are diagnosed before five years of age.[3] Some people with CGD do not have any identified genetic mutation. The cause of the condition in these individuals is unknown.[4] Mutations in the *CYBA*, *CYBB*, *NCF1*, *NCF2*, or *NCF4* gene can cause CGD.

The American Academy of Allergy, Asthma & Immunology and the American College of Allergy, Asthma & Immunology have jointly accepted responsibility for establishing the practice parameter for the diagnosis and management of primary immunodeficiency.[5] The practice parameter recommends patients with CGD be given prophylaxis with antimicrobial agents and Actimmune.

Severe, Malignant Osteopetrosis

SMO is an inherited disorder characterized by an osteoclast defect, leading to bone density overgrowth, and by deficient phagocyte oxidative metabolism. This leads to accumulation of bone with defective structure, making them brittle and susceptible to fracture. In some cases, this is also accompanied by skeletal abnormalities.[7] About 30% of all cases of osteopetrosis the cause of the condition is unknown, however, nine gene-related mutations are associated with osteopetrosis (*CA2*, *CLCN7*, *IKBKG*, *ITGB3*, *OSTM1*, *PLEKHM1*, *TCIRG1*, *TNFRSF11A*, *TNFSF11*).[8] The Osteopetrosis Working Group developed expert consensus guidelines for the diagnosis and management of osteopetrosis.[9] The guidelines recommend diagnosis is determined 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 the indication pertains only to severe infantile osteopetrosis.

POLICY STATEMENT

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 the following criteria:

FDA-Approved Indications

1. **Chronic Granulomatous Disease.** Approve for 1 year if the patient meets of the following criteria (A and B):
   - **A)** Diagnosis has been established by a molecular genetic test identifying a gene-related mutation linked to chronic granulomatous disease; AND
     Note: Examples of gene-related mutations 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.

2. **Malignant Osteopetrosis, Severe Infantile.** Approve for 1 year if the patient meets of the following criteria (A and B):
   - **A)** Diagnosis has been established by ONE of the following (i or ii)
     - **i.** Patient has had a radiographic (X-ray) imaging demonstrating skeletal features related to osteopetrosis; OR
     - **ii.** Patient has had a molecular genetic test identifying a gene-related mutation linked to severe, infantile malignant osteopetrosis; AND
   - **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 Pharma USA; October 2020.
2. Arnold D, Heimall J. A review of chronic granulomatous disease. *Advanced Therapy*. 2017;34:2543-2557.
3. Genetic Testing Registry. National Center for Biotechnology Information. Available at https://www.ncbi.nlm.nih.gov/gtr/conditions/C1856245/. Accessed on March 30, 2021.
4. Genetics Home Reference. National Institutes of Health, U.S. National Library of Medicine. Available at https://ghr.nlm.nih.gov/. Accessed on March 30, 2021. Search terms: chronic granulomatous disease.
5. 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.
6. Yu J, Azar A, Chong H, et al. Considerations in the diagnosis of chronic granulomatous disease. *Journal of the Pediatric Infectious Disease Society*. 2018;7:S6-S11.
7. Stark Z, Savarirayan R. Osteopetrosis. *Orphanet Journal of Rare Diseases*. 2009;4:5.

8. Genetics Home Reference. National Institutes of Health, U.S. National Library of Medicine. Available at https://ghr.nlm.nih.gov/. Accessed on March 30, 2021. Search terms: osteopetrosis.
9. Wu C, Econs M, DiMeglio L, et al. Diagnosis and management of osteopetrosis: consensus guidelines from the osteopetrosis working group. *The Journal of Clinical Endocrinology & Metabolism*. 2017;102:9:3111-3123.