Clinical Policy: Interferon Gamma-1b (Actimmune)

Reference Number: CP.PHAR.52
Effective Date: 06/10
Last Review Date: 05/17

Coding Implications
Revision Log

See Important Reminder at the end of this policy for important regulatory and legal information.

Description
The intent of the criteria is to ensure that patients follow selection elements established by Centene® clinical policy for interferon gamma-1b (Actimmune®).

Policy/Criteria
It is the policy of health plans affiliated with Centene Corporation® that Actimmune is **medically necessary** when the following criteria are met:

I. Initial Approval Criteria

A. Chronic Granulomatous Disease (must meet all):
1. Age ≥ 1 year;
2. Diagnosis of chronic granulomatous disease (CGD) confirmed with a neutrophil function test followed by immunoblot or genotyping;
3. Prescribed dose does not exceed one of the following:
   a. If body surface area is > $0.5m^2$, dose does not exceed $50mcg/m^2$ three times weekly;
   b. If body surface area is ≤ $0.5m^2$, dose does not exceed 1.5mcg/kg three times weekly.

Approval duration: 6 months

B. Severe Malignant Osteopetrosis (must meet all):
1. Age ≥ 1 month;
2. Diagnosis of severe malignant osteopetrosis (SMO) (also known as autosomal recessive osteopetrosis) confirmed by radiographic imaging;
3. Prescribed dose does not exceed one of the following:
   a. If body surface area is > $0.5m^2$, dose does not exceed $50mcg/m^2$ three times weekly;
   b. If body surface area is ≤ $0.5m^2$, dose does not exceed 1.5mcg/kg three times weekly.

Approval duration: 6 months

C. Other diagnoses/indications: Refer to CP.PHAR.57 - Global Biopharm Policy
1. The following NCCN recommended uses, meeting NCCN categories 1, 2a, or 2b, are approved per the CP.PHAR.57 Global Biopharm Policy:
   a. Mycosis fungoides/Sezary syndrome - Non-Hodgkin lymphomas.

Approval duration: 6 months

II. Continued Approval

A. Chronic Granulomatous Disease (must meet all):

1. Currently receiving medication via Centene benefit or member has previously met all initial approval criteria;
2. Demonstrated reduction in frequency and severity of serious infections associated with CGD;
3. Prescribed dose does not exceed one of the following:
   a. If body surface area is > $0.5m^2$, dose does not exceed $50mcg/m^2$ three times weekly;
   b. If body surface area is ≤ $0.5m^2$, dose does not exceed 1.5mcg/kg three times weekly.

Approval duration: 6 months

B. Malignant Osteopetrosis (must meet all):

1. Currently receiving medication via Centene benefit or member has previously met all initial approval criteria;
2. Member has not experienced disease progression while on therapy;
3. Prescribed dose does not exceed one of the following:
   a. If body surface area is > $0.5m^2$, dose does not exceed $50mcg/m^2$ three times weekly;
   b. If body surface area is ≤ $0.5m^2$, dose does not exceed 1.5mcg/kg three times weekly.

Approval duration: 6 months

C. Other diagnoses/indications (1 or 2):

1. Currently receiving medication via Centene benefit and documentation supports positive response to therapy.
   Approval duration: Duration of request or 6 months (whichever is less); or

2. Refer to CP.PHAR.57 - Global Biopharm Policy.

Background

Description/Mechanism of Action:

Actimmune (interferon gamma-1b), an interferon gamma, is a single-chain polypeptide containing 140 amino acids. Production of Actimmune is achieved by fermentation of a genetically engineered Escherichia coli bacterium containing the DNA which encodes for the recombinant protein. Interferons bind to specific cell surface receptors and initiate a sequence of intracellular events that lead to the transcription of interferon-stimulated genes. The three major groups of interferons (alpha, beta, and gamma) have partially overlapping biological activities that include immunoregulation such as increased resistance to microbial pathogens and inhibition of cell proliferation. Type 1 interferons (alpha and beta) bind to the alpha/ beta receptor. Interferon gamma binds to a different cell surface receptor and is classified as Type 2 interferon. Specific effects of interferon gamma include the enhancement of the oxidative metabolism of

macrophages, antibody dependent cellular cytotoxicity, activation of natural killer cells, and the expression of Fc receptors and major histocompatibility antigens.

- CGD is an inherited disorder of leukocyte function caused by defects in the enzyme complex responsible for phagocyte superoxide generation. Actimmune does not increase phagocyte superoxide production even in treatment responders.
- In SMO (an inherited disorder characterized by an osteoclast defect, leading to bone overgrowth, and by deficient phagocyte oxidative metabolism), a treatment-related enhancement of superoxide production by phagocytes was observed. Actimmune was found to enhance osteoclast function in vivo.

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.

Formulations:
Actimmune (interferon gamma-1b) is supplied as a solution in single-use vials for subcutaneous injection. Each vial permits the extraction of up to 0.5 mL of Actimmune with additional volume to facilitate solution withdrawal. Each 0.5 mL of Actimmune contains: 100 mcg (2 million International Units) of interferon gamma-1b. Supplied in one- or 12-vial cartons.

FDA Approved Indications:
Actimmune is an interferon gamma/subcutaneous injectable formulation indicated for:
- Reducing the frequency and severity of serious infections associated with CGD;
- Delaying time to disease progression in patients with SMO.

Appendices
Appendix A: Abbreviation Key
CGD: chronic granulomatous disease
SMO: severe, malignant osteopetrosis

Coding Implications
Codes referenced in this clinical policy are for informational purposes only. Inclusion or exclusion of any codes does not guarantee coverage. Providers should reference the most up-to-date sources of professional coding guidance prior to the submission of claims for reimbursement of covered services.

HCPCS Codes	Description
J9216	Injection, interferon, gamma 1-b, 3 million units

Reviews, Revisions, and Approvals	Date	Approval Date
Converted to Centene Clinical Policy Template	06/13	06/13

Reviews, Revisions, and Approvals	Date	Approval Date
Added Background information Added breast feeding to algorithm	06/14	06/14
Included efficacy data for both indications. Added contraindication, caution and dose adjustment information. Updated "Figure 1. Actimmune Algorithm" by including hypersensitivity question and removing breastfeeding question. Added Appendix A: Safety Concerns. Reviewed references; added reference number 8 for RCT information.	04/15	04/15
Policy converted to new template. Age added per PI; diagnostic confirmation method supported by UptoDate. SMO: dosing and age added per PI; definition of SMO added (autosomal recessive osteopetrosis (ARO); examples of "severe" added; confirmation by radiographic imaging added.	04/16	05/16
Hypersensitivity contraindication removed. NCCN compendial uses added. Approval duration added to "other indications" section under continuation of therapy.	04/17	05/17

References

1. Actimmune Prescribing Information. Lake Forest, IL: HZNP USA, Inc., July 2016. Available at: www.actimmune.com. Accessed April 17, 2017.
2. Rosenzweig SD, Holland SM. Chronic granulomatous disease: Pathogenesis, clinical manifestations, and diagnosis. In: UpToDate, Waltham, MA: Walters Kluwer Health; 2017. Available at uptodate.com. Accessed April 17, 2017.
3. Stark Z, Savarirayan R. Osteopetrosis. *Orphanet J Rare Dis.* 2009; 4(5): 1-12.
4. Wilson CJ, Vellodi A. Autosomal recessive osteopetrosis: diagnosis, management, and outcome. *Arch Dis Child.* 2000; 83(5): 449-452.
5. Key LL Jr, Rodriguiz RM, Willi SM, et al. Long-term treatment of osteopetrosis with recombinant human interferon gamma. *N Engl J Med.* 1995; 332(24): 1594-1599.

are subject to all terms, conditions, exclusions and limitations of the coverage documents (e.g., evidence of coverage, certificate of coverage, policy, contract of insurance, etc.), as well as to state and federal requirements and applicable Health Plan-level administrative policies and procedures.

This clinical policy is effective as of the date determined by the Health Plan. The date of posting may not be the effective date of this clinical policy. This clinical policy may be subject to applicable legal and regulatory requirements relating to provider notification. If there is a discrepancy between the effective date of this clinical policy and any applicable legal or regulatory requirement, the requirements of law and regulation shall govern. The Health Plan retains the right to change, amend or withdraw this clinical policy, and additional clinical policies may be developed and adopted as needed, at any time.

This clinical policy does not constitute medical advice, medical treatment or medical care. It is not intended to dictate to providers how to practice medicine. Providers are expected to exercise professional medical judgment in providing the most appropriate care, and are solely responsible for the medical advice and treatment of members. This clinical policy is not intended to recommend treatment for members. Members should consult with their treating physician in connection with diagnosis and treatment decisions.

Providers referred to in this clinical policy are independent contractors who exercise independent judgment and over whom the Health Plan has no control or right of control. Providers are not agents or employees of the Health Plan.

This clinical policy is the property of the Health Plan. Unauthorized copying, use, and distribution of this clinical policy or any information contained herein are strictly prohibited. Providers, members and their representatives are bound to the terms and conditions expressed herein through the terms of their contracts. Where no such contract exists, providers, members and their representatives agree to be bound by such terms and conditions by providing services to members and/or submitting claims for payment for such services.

Note: For Medicaid members, when state Medicaid coverage provisions conflict with the coverage provisions in this clinical policy, state Medicaid coverage provisions take precedence. Please refer to the state Medicaid manual for any coverage provisions pertaining to this clinical policy.

Note: For Medicare members, to ensure consistency with the Medicare National Coverage Determinations (NCD) and Local Coverage Determinations (LCD), all applicable NCDs, LCDs, and Medicare Coverage Articles should be reviewed prior to applying the criteria set forth in this clinical policy. Refer to the CMS website at http://www.cms.gov for additional information.