RXADVANCE
2 Park Central Drive
Southborough, MA 01772

Clinical Policy Title: **Interferon Gamma- 1b (Actimmune®)**
Policy Number: **RxA.22**
Drug(s) Applied: **Interferon gamma-1b (Actimmune®)**
Last Review Date: **04/2020**
Line of Business: **Commercial, HIM, Medicaid**

Background

Interferon gamma-1b (Actimmune®) is a recombinant form of gamma interferon. It is indicated for:

- Reducing the frequency and severity of serious infections associated with chronic granulomatous disease (CGD)
- Delaying time to disease progression in patients with severe, malignant osteopetrosis (SMO)

Indication	Dosing Regimen	Maximum Dose
CGD, SMO	BSA > 0.5 m^2: 50 mcg/m^2 SC three times weekly BSA ≤ 0.5 m^2: 1.5 mcg/kg/dose SC three times weekly	See dosing regimen

Single-use vial for injection: 100 mcg (2 million IU)/0.5 ml

Clinical Policy

Provider must submit documentation (such as office chart notes, lab results or other clinical information) supporting that the member has met all approval criteria.

I. Initial Approval Criteria

A. Chronic Granulomatous Disease (must meet all)**:**

1. Diagnosis of CGD;
2. Age 1 year of age or older;
3. Prescribed by or in consultation with a hematologist, immunologist or infectious disease specialist;
4. Dose does not exceed one of the following (a or b):
   a. Body surface area (BSA) > 0.5 m^2: 50 mcg/m^2 three times weekly;
   b. BSA ≤ 0.5 m^2: 1.5 mcg/kg three times weekly.

Approval duration:
Medicaid/HIM – 6 months
Commercial – 6 months or member's renewal period, whichever is longer

B. Severe Malignant Osteopetrosis (must meet all)**:**

1. Diagnosis of SMO (also known as autosomal recessive osteopetrosis);
2. Prescribed by or in consultation with an endocrinologist;
3. Age 1 month of age or older;
4. Dose does not exceed one of the following (a or b):
   a. BSA > 0.5 m^2: 50 mcg/m^2 three times weekly;
   b. BSA ≤ 0.5 m^2: 1.5 mcg/kg three times weekly.

Approval duration:
Medicaid/HIM – 6 months
Commercial – 6 months or member's renewal period, whichever is longer

C. Mycosis Fungoides (MF) and Sézary Syndrome (SS) (off-label) (must meet all)**:**

1. Diagnosis of MF or SS;
2. Prescribed by or in consultation with an oncologist;
3. Age 1 month of age or older;
4. Request meets one of the following (a, b, or c):
   a. BSA > 0.5 m^2: Dose does not exceed 50 mcg/m^2 three times weekly;
   b. BSA ≤ 0.5 m^2: Dose does not exceed 1.5 mcg/kg three times weekly;
   c. Dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (*prescriber must submit supporting evidence*).

Approval duration:
Medicaid/HIM – 6 months
Commercial – 6 months or member's renewal period, whichever is longer

II. Continued Therapy

A. All Indications in Section I (must meet all)**:**

1. Currently receiving medication that has been authorized by RxAdvance or member has previously met initial approval criteria listed in this policy;
2. Member is responding positively to therapy (e.g. no disease progression);
3. If request is for a dose increase, request meets one of the following (a, b, or c):
   a. BSA > 0.5 m^2: New dose does not exceed 50 mcg/ m^2 three times weekly;
   b. BSA ≤ 0.5 m^2: New dose does not exceed 1.5 mcg/kg three times weekly;
   c. New dose is supported by practice guidelines or peer-reviewed literature for the relevant off-label use (*prescriber must submit supporting evidence*).

Approval duration:
Medicaid/HIM – 6 months
Commercial – 6 months or member's renewal period, whichever is longer

III. Appendices

Appendix A: Abbreviation/Acronym Key
BSA: body surface area
CGD: chronic granulomatous disease
FDA: Food and Drug Administration
MF: Mycosis fungoides
NCCN: National Comprehensive Cancer Network
SC: Subcutaneous
SMO: severe, malignant osteopetrosis
SS: Sézary syndrome

Appendix B: Therapeutic Alternatives
Not applicable

Appendix C: Contraindications/Boxed Warnings

- Contraindication(s): Hypersensitivity to interferon gamma, *E. coli* derived products or any component of this product
- Boxed warning(s): None reported.

Appendix D: General Information

- The manufacturer's pivotal study for Actimmune® showed the drug offered no benefit versus placebo for primary study endpoints for idiopathic pulmonary fibrosis. Analysis of secondary endpoints demonstrated a trend toward increased overall survival in patients treated with Actimmune® with baseline forced vital capacity (FVC) > 70% of predicted. An analysis reported that patients with FVC > 55% also benefited.

However, the subgroup with FVC > 60% of predicted did not. Therefore, use of baseline FVC to predict benefit is at best speculative at this time.

- A second post-hoc analysis also indicated no benefit in mortality if a dose of > 100 mcg/m^2 was administered. Additional clarification of appropriate dosing needs to occur. Detailed data on cause of death was not provided. It is currently impossible to speculate that Actimmune® was the cause of reduced overall mortality. The absolute number of deaths differed by eight in the study.
- NCCN Compendium lists Actimmune® with a category 2A recommendation for the treatment of Mycosis fungoides and Sezary syndrome as primary therapy, treatment for refractory or progressive disease, or in combination with phototherapy, retinoids, or photopheresis.
- NCCN Compendium lists Actimmune® as a category 2B recommendation for stage IA and relapsed or persistent stage IA MF with B1 blood involvement.
- Positive response in CGD may include reduction in frequency and severity of serious infections associated with CGD or no disease progression while on therapy.

References

1. Actimmune Prescribing Information. Lake Forest, IL: Horizon Pharma USA, Inc.; May 2017. Available at: www.actimmune.com. Accessed October 25, 2018.
2. Stark Z, Savarirayan R. Osteopetrosis. *Orphanet J Rare Dis.* 2009; 4(5): 1-12.
3. Wilson CJ, Vellodi A. Autosomal recessive osteopetrosis: diagnosis, management, and outcome. *Arch Dis Child.* 2000; 83(5): 449-452.
4. 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.
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8. Actimmune Prescribing Information. Lake Forest, IL: Horizon Therapeutics USA; December 2019. Available at: https://hznp.azureedge.net/public/prescribing-information-actimmune.pdf. Accessed April 29, 2020.

Review/Revision History	Review/Revised Date	P&T Approval Date
Policy was established.	01/2020	02/07/2020
Policy reviewed & updated.	04/29/2020	05/20/2020