Clinical Policy Title:	interferon gamma- 1b
Policy Number:	RxA.22
Drug(s) Applied:	Actimmune®
Original Policy Date:	02/07/2020
Last Review Date:	03/09/2021
Line of Business Policy Applies to:	All lines of business

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)

Dosing Information

Drug Name	Indication	Dosing Regimen	Maximum Dose
interferon gamma-1b (Actimmune®)	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	50mcg/m^2

Dosage Forms

- 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 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 and older;
3. Prescribed by or in consultation with a hematologist, immunologist, oncologist, gastroenterologist, 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

Commercial: 6 months

This clinical policy has been developed to authorize, modify, or determine coverage for individuals with similar conditions. Specific care and treatment may vary depending on individual need and benefits covered by the plan. This policy is not intended to dictate to providers how to practice medicine, nor does it constitute a contract or guarantee regarding payment or results. This document may contain prescription brand name drugs that are trademarks of pharmaceutical manufacturers that are not affiliated with RxAdvance.

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Medicaid: 6 months

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

1. Diagnosis of SMO (also known as marble bone disease or malignant infantile osteopetrosis (MIOP));
2. Prescribed by or in consultation with an endocrinologist or rheumatologist;
3. Age 1 month and older;
4. Request meets one of the following (a, b, or c):
   a. BSA > 0.5 m2: Dose does not exceed 50 mcg/m2 three times weekly;
   b. BSA ≤ 0.5 m2: 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
Commercial: 6 months
Medicaid: 6 months

C. Mycosis Fungoides (MF) and Sezary 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 and 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
Commercial: 6 months
Medicaid: 6 months

II. Continued Therapy Approval

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
Commercial: 6 months
Medicaid: 6 months

III. Appendices

APPENDIX A: Abbreviation/Acronym Key

BSA: body surface area
CGD: chronic granulomatous disease
MF: Mycosis fungoides
NCCN: National Comprehensive Cancer Network

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SC: Subcutaneous
SMO: severe, malignant osteopetrosis
SS: Sezary 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 the 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.
- Bacillus Calmette-Guerrin (BCG) vaccination is contraindicated in CGD.

References

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9. Interferon Gamma-1b, Lexi-Drug. Lexicomp. Wolters Kluwer Health, Inc. Riverwoods, IL. Accessed with subscription at: http://online.lexi.com. Accessed January 23, 2021.

Review/Revision History	Review/Revision Date	P&T Approval Date
Policy established.	01/2020	02/07/2020
Policy reviewed & updated.	04/29/2020	05/20/2020
Policy was reviewed: 1. Policy title table was updated: Clinical Policy Title was updated to 'interferon gamma- 1b', Drug(s) Applied was updated to 'Actimmune®', Line of business policy applies was updated to All lines of business. 2. Dosing information: Drug name was added. 3. Initial approval criteria I.B.2 was updated as Prescribed by or in consultation with an endocrinologist or rheumatologist. 4. Continued therapy approval criteria II.A.1 was rephrased to "Currently receiving medication that has been authorized by RxAdvance…". 5. Commercial approval durations were updated to 6 months from 6 months or to the member's renewal date, whichever is longer. Approval duration for HIM was removed. 6. Appendix A was updated. 7. Appendix D was updated. 8. References were updated.	01/25/2021	03/09/2021

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