CARECONTINUUM™

# UTILIZATION MANAGEMENT MEDICAL POLICY

**POLICY:** Gamifant Utilization Management Medical Policy
- Gamifant® (emapalumab-lzsg intravenous infusion – Sobi)

**REVIEW DATE:** 01/08/2025

## OVERVIEW

Gamifant, an anti-interferon gamma (IFN-γ) antibody, is indicated for the treatment of **primary hemophagocytic lymphohistiocytosis** (HLH) in adult and pediatric patients with refractory, recurrent, or progressive disease, or intolerance with conventional HLH therapy.[1]

### Disease Overview

HLH is a syndrome characterized by signs and symptoms of extreme inflammation, caused by defects in cytotoxic function (cytotoxic T cells and natural killer cells).[2] The incidence is estimated at 1.2 cases per million individuals per year, but this is likely an underestimate.[3] In healthy individuals, cytotoxic function is important to terminate immune responses when appropriate by targeting and destroying activated immune cells. Deficiencies in cytotoxic function lead to an unchecked immune response and hyper-inflammation. Primary HLH has a clear genetic cause, whereas secondary HLH is triggered by a concomitant infection or medical condition, such as Epstein-Barr virus infection, malignancy, or rheumatologic disorders. IFN-γ normally has both pro-inflammatory functions (e.g., macrophage activation) and anti-inflammatory functions (e.g., activation of cytotoxic cells).[4,5] However, in HLH, the anti-inflammatory action of IFN-γ is ineffective due to impaired cytotoxic cell activity; thus, pro-inflammatory effects predominate.

### Guidelines

The HLH-2004 treatment protocol, developed by the Histiocyte Society, is the current standard of care for diagnostic and therapeutic guidelines.[6] Gamifant is not addressed in the 2004 protocol. To establish a diagnosis of HLH, patients must either have a molecular diagnosis consistent with HLH or must meet five out of eight diagnostic criteria. A backbone of etoposide and systemic dexamethasone is the conventional standard of care to induce symptomatic resolution; cyclosporine A and anti-thymocyte globulin have also demonstrated efficacy. Although chemotherapy prolongs survival in primary HLH, a hematopoietic stem cell transplant (HSCT) is needed for cure. Patients with primary HLH should continue chemotherapy (usually with etoposide, cyclosporine A, and dexamethasone) until HSCT can be performed. Myelotoxicity due to chemotherapy is a concern, especially since patients with HLH can have severe cytopenias and immunodeficiency at baseline.

## POLICY STATEMENT

Prior Authorization is recommended for medical benefit coverage of Gamifant. Approval is recommended for those who meet the **Criteria** and **Dosing** for the listed indication. Requests for doses outside of the established dosing documented in this policy will be considered on a case-by-case basis by a clinician (i.e., Medical Director or Pharmacist). All approvals are provided for the duration noted below. In cases where the approval is authorized in months, 1 month is equal to 30 days. Because of the specialized skills required for evaluation and diagnosis of patients treated with Gamifant, approval requires it to be prescribed by or in consultation with a physician who specializes in the condition being treated.

**Automation:** None.

## RECOMMENDED AUTHORIZATION CRITERIA

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

**FDA-Approved Indication**

1. **Hemophagocytic Lymphohistiocytosis, Primary.** Approve Gamifant for 6 months if the patient meets the following (A, B, C, and D):
   - **A)** Patient has a diagnosis of hemophagocytic lymphohistiocytosis determined by at least ONE of the following (i or ii):
     - **i.** Patient has a molecular genetic diagnosis consistent with hemophagocytic lymphohistiocytosis; OR
     - **ii.** Prior to treatment, the patient meets at least FIVE of the following diagnostic criteria at baseline (FIVE of a, b, c, d, e, f, g, or h):
       - **a)** Fever ≥ 38.5° C;
       - **b)** Splenomegaly;
       - **c)** Cytopenias defined as at least TWO of the following (TWO of 1, 2, or 3):
         - **1)** Hemoglobin < 9 g/dL (or < 10 g/dL in infants less than 4 weeks of age);
         - **2)** Platelets < 100 x $10^9$/L;
         - **3)** Neutrophils < 1.0 x $10^9$/L;
       - **d)** Patient meets ONE of the following (1 or 2):
         - **1)** Fasting triglycerides ≥ 265 mg/dL; OR
         - **2)** Fibrinogen ≤ 1.5 g/L;
       - **e)** Hemophagocytosis in bone marrow, spleen, or lymph nodes;
       - **f)** Low or absent natural killer cell activity (according to local laboratory reference);
       - **g)** Ferritin ≥ 500 mcg/L;
       - **h)** Soluble CD25 (i.e., soluble interleukin-2 receptor) ≥ 2,400 U/mL; AND
   - **B)** Patient has tried at least one conventional therapy (e.g., etoposide, cyclosporine A, or anti-thymocyte globulin); AND
   - **C)** According to the prescriber, the patient has experienced at least one of the following (i or ii):
     - **i.** Refractory, recurrent, or progressive disease during conventional therapy (e.g., etoposide, cyclosporine A, or anti-thymocyte globulin); OR
     - **ii.** Intolerance to conventional therapy (e.g., etoposide, cyclosporine A, or anti-thymocyte globulin); AND
   - **D)** The medication is prescribed by or in consultation with a hematologist, oncologist, immunologist, transplant specialist, or physician who specializes in hemophagocytic lymphohistiocytosis or related disorders.

   **Dosing.** Approve up to a maximum dose of 10 mg/kg by intravenous infusion, not more frequently than twice weekly (once every 3 to 4 days).

## CONDITIONS NOT RECOMMENDED FOR APPROVAL

Coverage of Gamifant 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. Gamifant® intravenous infusion [prescribing information]. Waltham, MA: Sobi; June 2023.
2. Jordan MB, Allen CE, Weitzman S, Filipovich AH, McClain KL. How I treat hemophagocytic lymphohistiocytosis. *Blood*. 2011;118(15):4041-4052.
3. Weitzman S. Approach to hemophagocytic syndromes. *Hematology Am Soc Hematol Edu Program.* 2011;2011:178-183.
4. Avau A, Matthys P. Therapeutic potential of interferon-γ and its antagonists in autoinflammation: lessons from murine models of systemic juvenile idiopathic arthritis and macrophage activation syndrome. *Pharmaceuticals.* 2015;8:793-815.
5. Osinska I, Popko K, Demkow U. Perforin: an important player in immune response. *Centr Eur J Immunol*. 2014;39(1):109-115.
6. Henter J, Horne A, Aricó M, et al. HLH-2004: Diagnostic and Therapeutic Guidelines for Hemophagocytic Lymphohistiocytosis. *Pediatr Blood Cancer*. 2007;48:124-131.

## HISTORY

| Type of Revision | Summary of Changes | Review Date |
|---|---|---|
| Annual Revision | No criteria changes. | 02/14/2024 |
| Annual Revision | No criteria changes. | 01/08/2025 |