Gamifant® (emapalumab-lzsg)

When requesting Gamifant® (emapalumab-lzsg), the individual requiring treatment must be diagnosed with one of the following FDA-approved indications and meet the specific coverage guidelines and applicable safety criteria for the covered indications.

FDA-Approved Indications

- Primary hemophagocytic lymphohistiocytosis (HLH) in adult and pediatric patients with refractory, recurrent, or progressive disease, or intolerance with conventional HLH therapy.
- Hemophagocytic Lymphohistiocytosis /Macrophage Activation Syndrome (HLH/MAS) in adult and pediatric patients with known or suspected Still's disease including systemic juvenile idiopathic arthritis (sJIA), with an inadequate response or intolerance to glucocorticoids, or with recurrent MAS.

Coverage Guidelines

Primary Hemophagocytic Lymphohistiocytosis

The individual must meet ALL of the following criteria for approval:

- Diagnosis has been determined by at least one of the following:
  - Has a molecular genetic diagnosis consistent with primary hemophagocytic lymphohistiocytosis;
  - Prior to treatment, the patient meets at least FIVE of the following diagnostic criteria at baseline:
    - Fever ≥ 38.5° C;
    - Splenomegaly;
    - Cytopenias defined as at least TWO of the following:
      - Hemoglobin < 9 g/dL (or < 10 g/dL in infants less than 4 weeks of age);
      - Platelets < 100 x 10^9/L;
      - Neutrophils < 1.0 x 10^9/L;
    - Fasting triglycerides ≥ 265 mg/dL OR fibrinogen ≤ 1.5 g/L;
    - Hemophagocytosis in bone marrow, spleen, or lymph nodes;
    - Low or absent natural killer cell activity (according to local laboratory reference);
    - Ferritin ≥ 500 mcg/L;
    - Soluble CD25 (i.e., soluble interleukin-2 receptor) ≥ 2,400 U/mL;
- Has tried at least one conventional therapy (e.g., etoposide, cyclosporine A, or anti-thymocyte globulin);
- Has experienced at least one of the following:
  - Refractory, recurrent, or progressive disease during conventional therapy (e.g., etoposide, cyclosporine A, or anti-thymocyte globulin)

    - Intolerance to conventional therapy (e.g., etoposide, cyclosporine A, or anti-thymocyte globulin)
- Prescribed by or in consultation with a hematologist, oncologist, immunologist, transplant specialist, or physician who specializes in hemophagocytic lymphohistiocytosis or related disorders.

Approval duration: 6 months

Hemophagocytic Lymphohistiocytosis /Macrophage Activation Syndrome (HLH/MAS)
Note: HLH/MAS is a form of secondary HLH

The individual must meet ALL of the following criteria for approval:
- Has a confirmed or suspected diagnosis of systemic juvenile idiopathic arthritis or Still's disease, adult onset;
- Prior to treatment, patient has a ferritin level > 684 ng/mL and at least TWO of the following diagnostic criteria at baseline;
    - Platelets ≤ 181 x 10^9/L;
    - AST > 48 U/L;
    - Fasting triglyceride > 156 mg/dL;
    - Fibrinogen ≤ 360 mg/dL;
- Meets one of the following:
    - Has had an inadequate response or intolerance to high dose intravenous corticosteroids;
    - Has previously received therapy with Gamifant
- Prescribed by or in consultation with a hematologist, oncologist, immunologist, rheumatologist, or physician that specializes in hemophagocytic lymphohistiocytosis or related disorders.

Approval duration: 8 weeks

Dosing Recommendations

Primary HLH
The recommended starting dosage is 1 mg/kg as an intravenous infusion over 1 hour twice per week. The dose may be titrated up to a maximum of 10 mg/kg.

HLH/MAS
The recommended starting dose is 6 mg/kg, followed by 3 mg/kg every 3 days for 5 doses, then 3 mg/kg twice per week given as an intravenous infusion over 1 hour. The dose may be titrated up to a maximum of 10 mg/kg.

References

1. Gamifant® intravenous infusion [prescribing information]. Waltham, MA: Sobi; June 2025.

2. Henter JI. Hemophagocytic Lymphohistiocytosis. *N Engl J Med.* 2025 Feb 6;392(6):584-598.
3. Konkol S, Killeen RB, Rai M. Hemophagocytic Lymphohistiocytosis. [Updated 2025 May 3]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2025 Jan-. Available from: https://www.ncbi.nlm.nih.gov/books/NBK557776/. Accessed on: July 7, 2025.
4. Henter J, Horne A, Aricó M, et al. HLH-2004: Diagnostic and Therapeutic Guidelines for Hemophagocytic Lymphohistiocytosis. *Pediatr Blood Cancer*. 2007;48:124-131.
5. Fautrel B, Mitrovic S, De Matteis A, et al. EULAR/PReS recommendations for the diagnosis and management of Still's disease, comprising systemic juve nile idiopathic arthritis and adult-onset Still's disease. *Ann Rheum Dis.* 2024;83(12):1614-1627.

