Clinical Policy: Emapalumab-lzsg (Gamifant)

Reference Number: PA.CP.PHAR.402
Effective Date: 01/2019
Last Review Date: 07/2025

Description
Emapalumab-lzsg (Gamifant™) is an interferon gamma (IFNγ) blocking antibody.

FDA Approved Indication(s)
Gamifant is indicated for the treatment of:

- Adult and pediatric (newborn and older) patients with primary hemophagocytic lymphohistiocytosis (HLH) with refractory, recurrent or progressive disease or intolerance with conventional HLH therapy.
- Adult and pediatric (newborn and older) patients with HLH/macrophage activation syndrome (MAS) in known or suspected Still's disease, including systemic juvenile idiopathic arthritis (sJIA), with an inadequate response or intolerance to glucocorticoids, or with recurrent MAS.

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

It is the policy of PA Health & Wellness® that Gamifant is **medically necessary** when the following criteria are met:

I. Initial Approval Criteria

A. Primary Hemophagocytic Lymphohistiocytosis (must meet all)**:**

1. Diagnosis of primary HLH (i.e., familial (inherited) HLH);
2. Prescribed by or in consultation with a hematologist or immunologist;
3. Failure of conventional HLH therapy that includes an etoposide- and dexamethasone-based regimen, unless contraindicated or clinically significant adverse effects are experienced;
4. Gamifant is prescribed in combination with dexamethasone;
5. Documentation of a scheduled bone marrow or hematopoietic stem cell transplantation (HSCT) or identification of a transplant donor is in process;
6. Dose does not exceed 10 mg/kg per dose, two doses per week.

Approval duration: 2 months

B. Hemophagocytic Lymphohistiocytosis/Macrophage Activation Syndrome in Still's Disease (must meet all)**:**

1. Diagnosis of both of the following (a and b):
   a. HLH/MAS;
   b. Still's disease (including sJIA);
2. Prescribed by or in consultation with an immunologist, rheumatologist, or hematologist;

3. Member has active MAS confirmed by all the following (a, b, and c) assessed within the last 30 days:
   a. Fever (oral temperature > 100.4°F);
   b. Ferritin > 684 ng/mL;
   c. Two of the following laboratory criteria:
      i. Platelets ≤ 181×10^9 /L;
      ii. Aspartate aminotransferase (AST) > 48 U/L;
      iii. Triglycerides > 156 mg/dL;
      iv. Fibrinogen ≤ 360 mg/dL;
4. Inadequate response to high-dose intravenous corticosteroid (*see Appendix B*), unless contraindicated or clinically significant adverse effects are experienced;
5. Gamifant is prescribed in combination with a corticosteroid;
6. Dose does not exceed both of the following (a and b):
   a. All of the following (i, ii, and iii):
      i. Day 1: 6 mg/kg;
      ii. Days 4 to 16: 3 mg/kg every 3 days for 5 doses;
      iii. Day 19 onward: 3 mg/kg twice per week (i.e., every 3 to 4 days);
   b. If member has unsatisfactory improvement with the above dosing: cumulative dose of 10 mg/kg over 3 days.

Approval duration: 2 months

C. Other diagnoses/indications

1. Refer to the off-label use policy for the relevant line of business if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): PA.CP.PMN.53.

II. Continued Therapy

A. Primary Hemophagocytic Lymphohistiocytosis (must meet all)**:**

1. Currently receiving medication via PA Health & Wellness benefit or member has previously met initial approval criteria or the Continuity of Care policy (PA.PHARM.01) applies;
2. Member is responding positively to therapy – including but not limited to improvement in <u>any</u> of the following parameters:
   a. Fever reduction;
   b. Splenomegaly;
   c. Central nervous system symptoms;
   d. Complete blood count;
   e. Fibrinogen and/or D-dimer;
   f. Ferritin;
   g. Soluble CD25 (also referred to as soluble interleukin-2 receptor) levels;
3. Member has not yet received a successful bone marrow transplant or HSCT;
4. Gamifant is prescribed in combination with dexamethasone;
5. If request is for a dose increase, new dose does not exceed 10 mg/kg per dose, two doses per week.

Approval duration: 6 months

B. Hemophagocytic Lymphohistiocytosis/Macrophage Activation Syndrome in Still's Disease (must meet all)**:**

1. Currently receiving medication via PA Health & Wellness benefit or member has previously met initial approval criteria or the Continuity of Care policy (PA.PHARM.01) applies;
2. Member is responding positively to therapy – including but not limited to resolution of fever, improvements in physical examination (e.g., rash, arthritis, lymphadenopathy, resolving neurological symptoms, organ-specific findings), and laboratory abnormalities (e.g., cytopenias, transaminitis, hyperferritinemia);
3. If request is for a dose increase, new dose does not exceed one of the following (a or b):
    a. 3 mg/kg twice per week (i.e., every 3 to 4 days);
    b. If member has unsatisfactory improvement with the above dosing: cumulative dose of 10 mg/kg over 3 days.

Approval duration: 6 months

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

1. Currently receiving medication via PA Health & Wellness benefit and documentation supports positive response to therapy or the Continuity of Care policy (PA.PHARM.01) applies.
   Approval duration: Duration of request or 6 months (whichever is less); or
2. Refer to the off-label use policy for the relevant line of business if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): PA.CP.PMN.53.

III. Diagnoses/Indications for which coverage is NOT authorized:

A. Non-FDA approved indications, which are not addressed in this policy, unless there is sufficient documentation of efficacy and safety according to the off label use policy – PA.CP.PMN.53 or evidence of coverage documents.

IV. Appendices/General Information

Appendix A: Abbreviation/Acronym Key

FDA: Food and Drug Administration
HLH: hemophagocytic lymphohistiocytosis
HSCT: hematopoietic stem cell transplantation
MAS: macrophage activation syndrome
sJIA: systemic juvenile idiopathic arthritis

Appendix B: Therapeutic Alternatives

This table provides a listing of preferred alternative therapy recommended in the approval criteria. The drugs listed here may not be a formulary agent and may require prior authorization.

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
etoposide (Toposar®)	Primary HLH: 150 mg/m^2 IV twice weekly for 2 weeks and then weekly for an additional 6 weeks. Continuation therapy from week 9 until HSCT: 150 mg/m^2 every alternating second week	150 mg/m^2 per dose
dexamethasone	Primary HLH: 10 mg/m^2 PO or IV for 2 weeks followed by 5 mg/m^2 for 2 weeks, 2.5 mg/m^2 for 2 weeks, 1.25 mg/m^2 for 1 week, and 1 week of tapering Continuation therapy from week 9 until HSCT: 1010 mg/m^2 for 3 days every second week	See dosing regimen
Corticosteroids (e.g., prednisone, methylprednisolone, dexamethasone)	HLH/MAS: Varies* *In clinical trials for Gamifant in HLH/MAS (NCT03311854, NCT05001737), high-dose glucocorticoids were defined as ≥ 2 mg/kg/day of prednisone equivalent in two divided doses, or at least 60 mg/day in patients weighing 30 kg or more, including but not limited to pulses up to 30 mg/kg/day for at least 3 consecutive days	Varies

Therapeutic alternatives are listed as Brand name® (generic) when the drug is available by brand name only and generic (Brand name®) when the drug is available by both brand and generic.

Appendix C: Contraindications/Boxed Warnings
None reported

Appendix D: General Information
- Overall response in the Gamifant primary HLH clinical trial (NCT01818492) was evaluated using an algorithm that included the following objective clinical and laboratory parameters: fever, splenomegaly, central nervous system symptoms, complete blood count, fibrinogen and/or D-dimer, ferritin, and soluble CD25 (also referred to as soluble interleukin-2 receptor) levels.

- Complete response was defined as normalization of all HLH abnormalities (i.e., no fever, no splenomegaly, neutrophils > $1x10^9$/L, platelets > $100x10^9$/L, ferritin < 2,000 µg/L, fibrinogen > 1.50 g/L, D-dimer < 500 ug/L, normal CNS symptoms, no worsening of sCD25 > 2-fold baseline).
- Partial response was defined as normalization of ≥ 3 HLH abnormalities.
- HLH improvement was defined as ≥ 3 HLH abnormalities improved by at least 50% from baseline.

V. Dosage and Administration

Indication	Dosing Regimen	Maximum Dose
Primary HLH	Initial: 1 mg/kg IV twice per week (every three to four days) Subsequent doses may be increased based on clinical and laboratory criteria.	10 mg/kg/dose
HLH/MAS	Day 1: 6 mg/kg IV Days 4 to 16: 3 mg/kg IV every 3 days for 5 doses From Day 19 onward: 3 mg/kg IV twice per week (i.e., every 3 to 4 days) If member has unsatisfactory improvement with the above dosing, dose may be increased to a maximum cumulative dose of 10 mg/kg over 3 days and frequency may be increased to every 2 days or once daily.	See dosing regimen

VI. Product Availability

Single-dose vial: 10 mg/2 mL, 50 mg/10 mL, 100 mg/20 mL, 50 mg/2 mL, 100 mg/4 mL, 250 mg/10 mL, 500 mg/20 mL

VII. References

1. Gamifant Prescribing Information. Geneva, Switzerland: Novimmune; June 2025. Available at: https://www.gamifant.com/pdf/Full-Prescribing-Information.pdf. Accessed July 7, 2025.
2. Henter JI, Samuelsson-Horne AC, Arico M, et al. Treatment of hemophagocytic lymphohistiocytosis with HLH-94 immunochemotherapy and bone marrow transplantation. Blood 2002; 100 (7): 2367-72.
3. Chesshyre E, Ramanan AV, Roderick MR. Hemophagocytic Lymphohistiocytosis and Infections: An update. The Pediatric Infectious Disease Journal March 2019; 38(3): e54-e56.
4. Bergsten E, Horne AC, Arico M, et al. Confirmed efficacy of etoposide and dexamethasone in HLH treatment: long-term results of the cooperative HLH-2004 study. Blood 2017; 130 (25): 2728-38.
5. Locatelli F, Jordan MB, Allen C, et al. Emapalumab in Children with Primary Hemophagocytic Lymphohistiocytosis. N Engl J Med. 2020 May 7;382(19):1811-1822. doi: 10.1056/NEJMoa1911326. PMID: 32374962.
6. De Benedetti F, Grom AA, Brogan PA, et al. Efficacy and safety of emapalumab in macrophage activation syndrome. Ann Rheum Dis. 2023 Jun; 82(6): 857-865.

7. Ravelli A, Minoia F, Davì S, et al. 2016 classification criteria for macrophage activation syndrome complicating systemic juvenile idiopathic arthritis: a European League Against Rheumatism/American College of Rheumatology/Paediatric Rheumatology International Trials Organisation collaborative initiative. Arthritis Rheumatol 2016;68:566–76.
8. Evaluate Efficacy, Safety and Tolerability, PK and PD of Emapalumab in Children and Adults With MAS in Still's or SLE (EMERALD). ClinicalTrials.gov identifier: NCT05001737. Updated June 11, 2025. Available at: https://clinicaltrials.gov/study/NCT05001737. Accessed July 9, 2025.

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
J9210	Injection, emapalumab-lzsg, 1 mg

Reviews, Revisions, and Approvals	Date
Policy created	01/2019
1Q 2020 annual review: no significant changes; references reviewed and updated.	01/2020
1Q 2021 annual review: added criteria for diagnosis confirmation per clinical trial inclusion criteria; references reviewed and updated.	01/2021
1Q 2022 annual review: references reviewed and updated.	01/2022
1Q 2023 annual review: per prescribing information added requirement that Gamifant is prescribed in combination with dexamethasone, for continued therapy added requirement that member has not received a successful bone marrow transplant or HSCT; removed inactive HCPCS code C9050; references reviewed and updated.	01/2023
1Q 2024 annual review: added immunologist as an additional specialist prescriber; added requirement for concurrent use with dexamethasone to continuation of therapy; references reviewed and updated.	01/2024
1Q 2025 annual review: no significant changes; added additional vial sizes per updated prescribing information; references reviewed and updated; references reviewed and updated.	01/2025
RT4: added new indication for HLH/MAS per updated prescribing information.	07/2025