

## **Clinical Policy: Emapalumab-lzsg (Gamifant)**

Reference Number: CP.PHAR.402

Effective Date: 12.11.18

Last Review Date: 02.26

Line of Business: Commercial, HIM, Medicaid

[Coding Implications](#)  
[Revision Log](#)

See [Important Reminder](#) at the end of this policy for important regulatory and legal information.

### **Description**

Emapalumab-lzsg (Gamifant<sup>™</sup>) is an interferon gamma (IFN $\gamma$ ) 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 health plans affiliated with Centene Corporation<sup>®</sup> 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. Diagnosis is confirmed based on one of the following (a, b, or c):
  - a. Genetic mutation known to cause HLH (e.g., PRF1, UNC13D, STX11 and STXBP2);
  - b. Family history consistent with primary HLH;
  - c. Five of the following criteria are satisfied (1-8):
    - 1) Fever;
    - 2) Splenomegaly;
    - 3) Cytopenias affecting 2 of 3 lineages in the peripheral blood (hemoglobin < 9 g/dL (or < 10 g/dL in infants), platelets < 100 x 10<sup>9</sup> /L, neutrophils < 1 x 10<sup>9</sup>/L);
    - 4) Hypertriglyceridemia (fasting TG  $\geq$  3 mmol/L or  $\geq$  265 mg/dL) and/or hypofibrinogenemia (fibrinogen  $\leq$  1.5 g/L);
    - 5) Hemophagocytosis in bone marrow, spleen, or lymph nodes with no evidence of malignancy;
    - 6) Low or absent NK-cell activity;

- 7) Ferritin  $\geq$  500 mcg/L;
- 8) Soluble CD25 (sCD25; i.e., soluble IL-2 receptor)  $\geq$  2,400 U/mL;
3. Prescribed by or in consultation with a hematologist or immunologist;
4. Failure of conventional HLH therapy that includes an etoposide- and dexamethasone-based regimen, unless contraindicated or clinically significant adverse effects are experienced;
5. Gamifant is prescribed in combination with dexamethasone;
6. Documentation of a scheduled bone marrow or hematopoietic stem cell transplantation (HSCT) or identification of a transplant donor is in process;
7. 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  $\leq$   $181 \times 10^9$  /L;
    - ii. Aspartate aminotransferase (AST)  $>$  48 U/L;
    - iii. Triglycerides  $>$  156 mg/dL;
    - iv. Fibrinogen  $\leq$  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 (must meet 1 or 2):**

1. If this drug has recently (within the last 6 months) undergone a label change (e.g., newly approved indication, age expansion, new dosing regimen) that is not yet reflected in this policy, refer to one of the following policies (a or b):
  - a. For drugs on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the no coverage criteria policy for the relevant line of business:

- CP.CPA.190 for commercial, HIM.PA.33 for health insurance marketplace, and CP.PMN.255 for Medicaid; or
- b. For drugs NOT on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the non-formulary policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.103 for health insurance marketplace, and CP.PMN.16 for Medicaid; or
2. If the requested use (e.g., diagnosis, age, dosing regimen) is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized) AND criterion 1 above does not apply, refer to the off-label use policy for the relevant line of business: CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace, and CP.PMN.53 for Medicaid.

## II. Continued Therapy

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

1. Member meets one of the following (a or b):
  - a. Currently receiving medication via Centene benefit or member has previously met initial approval criteria;
  - b. Member is currently receiving medication and is enrolled in a state and product with continuity of care regulations (*refer to state specific addendums for CC.PHARM.03A and CC.PHARM.03B*);
2. Member is responding positively to therapy – including but not limited to improvement in any of the following parameters (a-g):
  - 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. Member meets one of the following (a or b):
  - a. Currently receiving medication via Centene benefit or member has previously met initial approval criteria;
  - b. Member is currently receiving medication and is enrolled in a state and product with continuity of care regulations (*refer to state specific addendums for CC.PHARM.03A and CC.PHARM.03B*);
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. If this drug has recently (within the last 6 months) undergone a label change (e.g., newly approved indication, age expansion, new dosing regimen) that is not yet reflected in this policy, refer to one of the following policies (a or b):
  - a. For drugs on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the no coverage criteria policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.33 for health insurance marketplace, and CP.PMN.255 for Medicaid; or
  - b. For drugs NOT on the formulary (commercial, health insurance marketplace) or PDL (Medicaid), the non-formulary policy for the relevant line of business: CP.CPA.190 for commercial, HIM.PA.103 for health insurance marketplace, and CP.PMN.16 for Medicaid; or
2. If the requested use (e.g., diagnosis, age, dosing regimen) is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized) AND criterion 1 above does not apply, refer to the off-label use policy for the relevant line of business: CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace, and CP.PMN.53 for Medicaid.

**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 policies – CP.CPA.09 for commercial, HIM.PA.154 for health insurance marketplace, and CP.PMN.53 for Medicaid, 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 for all relevant lines of business and may require prior authorization.*

| Drug Name                                                                | Dosing Regimen                                                                                                                                                                                                                                                                                                                                                  | Dose Limit/<br>Maximum Dose    |
|--------------------------------------------------------------------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|--------------------------------|
| etoposide<br>(Toposar <sup>®</sup> )                                     | Primary HLH:<br>150 mg/m <sup>2</sup> IV twice weekly for 2 weeks and then weekly for an additional 6 weeks.<br><br>Continuation therapy from week 9 until HSCT:<br>150 mg/m <sup>2</sup> every alternating second week                                                                                                                                         | 150 mg/m <sup>2</sup> per dose |
| dexamethasone                                                            | Primary HLH:<br>10 mg/m <sup>2</sup> PO or IV for 2 weeks followed by 5 mg/m <sup>2</sup> for 2 weeks, 2.5 mg/m <sup>2</sup> for 2 weeks, 1.25 mg/m <sup>2</sup> for 1 week, and 1 week of tapering<br><br>Continuation therapy from week 9 until HSCT:<br>1010 mg/m <sup>2</sup> for 3 days every second week                                                  | See dosing regimen             |
| Corticosteroids<br>(e.g., prednisone, methylprednisolone, dexamethasone) | HLH/MAS:<br>Varies*<br><br>*In clinical trials for Gamifant in HLH/MAS (NCT03311854, NCT05001737), high-dose glucocorticoids were defined as $\geq 2$ 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<sup>®</sup> (generic) when the drug is available by brand name only and generic (Brand name<sup>®</sup>) 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  $> 1 \times 10^9/L$ , platelets  $> 100 \times 10^9/L$ , ferritin  $< 2,000$   $\mu g/L$ , fibrinogen  $> 1.50$  g/L, D-dimer  $< 500$   $\mu g/L$ , normal CNS symptoms, no worsening of sCD25  $> 2$ -fold baseline).
  - Partial response was defined as normalization of  $\geq 3$  HLH abnormalities.
  - HLH improvement was defined as  $\geq 3$  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)<br>Subsequent doses may be increased based on clinical and laboratory criteria.                                                                                                                                                                                                                     | 10 mg/kg/dose      |
| HLH/MAS     | Day 1: 6 mg/kg IV<br>Days 4 to 16: 3 mg/kg IV every 3 days for 5 doses<br>From Day 19 onward: 3 mg/kg IV twice per week (i.e., every 3 to 4 days)<br><br>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 vials: 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 October 23, 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. Ravelli A, Minoia F, Davi 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.
7. 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.

8. Fautrel B, Mitrovic S, De Matteis et al. EULAR/PReS recommendations for the diagnosis and management of Still's disease, comprising systemic juvenile idiopathic arthritis and adult-onset Still's disease. *Ann Rheum Dis.* 2024 Nov 14;83(12):1614-1627. doi: 10.1136/ard-2024-225851.

**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     | P&T Approval Date |
|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|----------|-------------------|
| 1Q 2022 annual review: no significant changes; references reviewed and updated.                                                                                                                                                                                                                                           | 09.21.21 | 02.22             |
| Template changes applied to other diagnoses/indications and continued therapy section.                                                                                                                                                                                                                                    | 09.23.22 |                   |
| 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. | 10.13.22 | 02.23             |
| 1Q 2024 annual review: added examples of possible HLH related genetic mutations; added immunologist as an additional specialist prescriber; added requirement for concurrent use with dexamethasone to continuation of therapy; references reviewed and updated.                                                          | 10.06.23 | 02.24             |
| 1Q 2025 annual review: no significant changes; added additional vial sizes per updated prescribing information; references reviewed and updated; references reviewed and updated.                                                                                                                                         | 10.22.24 | 02.25             |
| RT4: added new indication for HLH/MAS per updated prescribing information.                                                                                                                                                                                                                                                | 07.07.25 | 08.25             |
| 1Q 2026 annual review: no significant changes; references reviewed and updated.                                                                                                                                                                                                                                           | 10.23.25 | 02.26             |

**Important Reminder**

This clinical policy has been developed by appropriately experienced and licensed health care professionals based on a review and consideration of currently available generally accepted standards of medical practice; peer-reviewed medical literature; government agency/program approval status; evidence-based guidelines and positions of leading national health professional organizations; views of physicians practicing in relevant clinical areas affected by this clinical

policy; and other available clinical information. The Health Plan makes no representations and accepts no liability with respect to the content of any external information used or relied upon in developing this clinical policy. This clinical policy is consistent with standards of medical practice current at the time that this clinical policy was approved. “Health Plan” means a health plan that has adopted this clinical policy and that is operated or administered, in whole or in part, by Centene Management Company, LLC, or any of such health plan’s affiliates, as applicable.

The purpose of this clinical policy is to provide a guide to medical necessity, which is a component of the guidelines used to assist in making coverage decisions and administering benefits. It does not constitute a contract or guarantee regarding payment or results. Coverage decisions and the administration of benefits are subject to all terms, conditions, exclusions, and limitations of the coverage documents (e.g., evidence of coverage, certificate of coverage, policy, contract of insurance, etc.), as well as to state and federal requirements and applicable Health Plan-level administrative policies and procedures.

This clinical policy is effective as of the date determined by the Health Plan. The date of posting may not be the effective date of this clinical policy. This clinical policy may be subject to applicable legal and regulatory requirements relating to provider notification. If there is a discrepancy between the effective date of this clinical policy and any applicable legal or regulatory requirement, the requirements of law and regulation shall govern. The Health Plan retains the right to change, amend or withdraw this clinical policy, and additional clinical policies may be developed and adopted as needed, at any time.

This clinical policy does not constitute medical advice, medical treatment, or medical care. It is not intended to dictate to providers how to practice medicine. Providers are expected to exercise professional medical judgment in providing the most appropriate care, and are solely responsible for the medical advice and treatment of members. This clinical policy is not intended to recommend treatment for members. Members should consult with their treating physician in connection with diagnosis and treatment decisions.

Providers referred to in this clinical policy are independent contractors who exercise independent judgment and over whom the Health Plan has no control or right of control. Providers are not agents or employees of the Health Plan.

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**Note:**

**For Medicaid members**, when state Medicaid coverage provisions conflict with the coverage provisions in this clinical policy, state Medicaid coverage provisions take precedence. Please refer to the state Medicaid manual for any coverage provisions pertaining to this clinical policy.



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