TRUECARE

PHARMACY POLICY STATEMENT
Mississippi Medicaid

DRUG NAME	Gamifant (emapalumab-lzsg)
BENEFIT TYPE	Medical
STATUS	Prior Authorization Required

Gamifant, approved by the FDA in 2018, is an interferon gamma (IFNγ) neutralizing antibody 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. It is the first FDA approved drug indicated for primary HLH.
Gamifant is also indicated to treat 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.
HLH is a rare, multi-organ syndrome characterized by immune dysregulation (of NK cells, CD8+ cytotoxic T cells, and macrophages) leading to hyperinflammation. Primary HLH is caused by genetic defects and typically manifests during infancy or early childhood. It is fatal if left untreated. The mainstay of treatment focuses on immunosuppression and cytotoxic therapy. The objective is to suppress inflammation to allow for stem cell transplant.
MAS is a secondary form of HLH, and is a severe, life-threatening complication of rheumatic diseases, most frequently in Still's disease (i.e., systemic juvenile idiopathic arthritis (sJIA) and adult-onset Still's disease (AOSD)). High-dose glucocorticoids are the main treatment.

Gamifant (emapalumab-lzsg) will be considered for coverage when the following criteria are met:

Primary Hemophagocytic Lymphohistiocytosis (HLH)

For **initial** authorization:

1. Medication must be prescribed by or in consultation with a hematologist; AND
2. Member has diagnosis of primary HLH with either refractory, recurrent, or progressive disease during conventional HLH therapy (e.g., dexamethasone with etoposide, cyclosporine A) or intolerance to conventional HLH therapy (Documentation required); AND
3. HLH diagnosis confirmed by ONE of the following:
   a) Genetic testing
   b) 5 out of 8 criteria fulfilled:
      i) Fever
      ii) Splenomegaly
      iii) Cytopenias affecting at least 2 of 3 peripheral cell lines (hemoglobin < 9 g/dL, platelets < 100 x 10^9/L, neutrophils < 1 x 10^9/L)
      iv) Hypertriglyceridemia (fasting triglycerides ≥ 265 mg/dL) and/or hypofibrinogenemia (≤ 1.5 g/L)
      v) Hemophagocytosis in bone marrow, spleen, or lymph nodes with no evidence of malignancy
      vi) Low or absent NK cell activity
      vii) Ferritin ≥ 500 mcg/L
      viii) Soluble CD25 (soluble IL-2 receptor) ≥ 2400 U/mL; AND
4. Medication will be administered concomitantly with dexamethasone; AND

5. Member does NOT have any of the following:
   a) Diagnosis of secondary HLH (e.g., consequent to a proven rheumatic or neoplastic disease)
   b) Active infection with mycobacteria, Histoplasma capsulatum, shigella, salmonella, campylobacter or leishmania; AND
6. Member must have a negative TB test within 12 months prior to starting therapy; AND
7. **Dosage allowed/Quantity limit:** Start with 1 mg/kg as an intravenous infusion twice per week; may increase based on clinical and laboratory criteria, per prescribing information, up to a max of 10 mg/kg.

If all the above requirements are met, the medication will be approved for 8 weeks.

For **reauthorization**:
1. Chart notes must show improvement of HLH parameters from baseline, including fever, splenomegaly, central nervous system symptoms, neutrophil count, platelet count, fibrinogen, D-dimer, ferritin, and/or soluble CD25 (also referred to as soluble interleukin-2 receptor) levels; AND
2. Member has not received a hematopoietic stem cell transplant since initial authorization.

If all the above requirements are met, the medication will be approved for an additional 6 months.

Hemophagocytic Lymphohistiocytosis/Macrophage Activation Syndrome (HLH/MAS) in Still's Disease

For **initial** authorization:
1. Medication must be prescribed by or in consultation with a rheumatologist; AND
2. Member has a documented diagnosis of HLH/MAS in known or suspected Still's Disease (including systemic Juvenile Idiopathic Arthritis (sJIA)); AND
3. Active MAS confirmed by all of the following:
   a) Ferritin >684 ng/mL, and
   b) 2 of the following:
      i) Platelet count ≤ 181 $x10^9$/L
      ii) AST >48 U/L
      iii) Triglycerides > 156 mg/dL
      iv) Fibrinogen level ≤ 360 mg/dL; AND
4. Member meets one of the following:
   a) inadequate response or intolerance to high dose glucocorticoids
   b) recurrent MAS
   c) severe MAS with rapid worsening or life-threatening MAS; AND
5. Member does NOT have any of the following:
   a) Diagnosis of Primary HLH
   b) Presence of malignancy; AND
6. Member must have a negative TB test within 12 months prior to starting therapy.
7. **Dosage allowed/Quantity limit:**

Treatment Day	GAMIFANT Dosage
Day 1	6 mg/kg
Days 4 to 16	3 mg/kg every 3 days for 5 doses
From Day 19 onward	3 mg/kg twice per week (i.e., every 3 to 4 days)

May increase based on clinical and laboratory criteria, per prescribing information, up to a cumulative max of 10 mg/kg over 3 days.

If all the above requirements are met, the medication will be approved for 8 weeks.

For **reauthorization**:

1. Chart notes must show response to treatment such as clinical resolution of MAS signs and symptoms and laboratory parameter endpoints.

If all the above requirements are met, the medication will be approved for an additional 8 weeks.

TrueCare considers Gamifant (emapalumab-lzsg) not medically necessary for the treatment of conditions that are not listed in this document. For any other indication, please refer to the Off-Label policy.

DATE	ACTION/DESCRIPTION
09/23/2019	New policy for Gamifant created.
09/21/2023	Updated template. Revised references. Rearranged numbering. Added starting dose. Removed MTX, hydrocortisone from conventional therapy since they are not always used; added cyclosporine. Shortened renewal duration from 12 months to 6 months. Removed concomitant disease exclusion. Removed family history as diagnostic verification.
07/22/2025	Primary HLH: Added reference (La Rosee 2019). Removed vaccine requirement. Removed body weight from list of exclusions. Removed malignancy from exclusion list (redundancy). Simplified renewal criteria. Added new indication of HLH/MAS.

References:

1. 2021 Georgia Code Title 33 – Insurance Chapter 20A - Managed Health Care Plans Article 2 - Patient's Right to Independent Review § 33-20A-31 Definitions. Justia US Law. Accessed April 25, 2023. https://law.justia.com/codes/georgia/2021/title-33/chapter-20a/article-2/section-33-20a-31/.
2. Gamifant [prescribing information]. Waltham, MA: Sobi Inc.; 2025.
3. Locatelli F, Jordan MB, Allen C, et al. Emapalumab in Children with Primary Hemophagocytic Lymphohistiocytosis. *N Engl J Med*. 2020;382(19):1811-1822. doi:10.1056/NEJMoa1911326
4. Henter JI, Horne A, Aricó M, et al. HLH-2004: Diagnostic and therapeutic guidelines for hemophagocytic lymphohistiocytosis. *Pediatr Blood Cancer*. 2007;48(2):124-131. doi:10.1002/pbc.21039
5. Konkol S, Rai M. Lymphohistiocytosis. [Updated 2023 Mar 27]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2023 Jan-. Available from: https://www.ncbi.nlm.nih.gov/books/NBK557776/

6. Jordan MB, Allen CE, Greenberg J, et al. Challenges in the diagnosis of hemophagocytic lymphohistiocytosis: Recommendations from the North American Consortium for Histiocytosis (NACHO). *Pediatr Blood Cancer*. 2019;66(11):e27929. doi:10.1002/pbc.27929
7. La Rosée P, Horne A, Hines M, et al. Recommendations for the management of hemophagocytic lymphohistiocytosis in adults. *Blood*. 2019;133(23):2465-2477. doi:10.1182/blood.2018894618
8. De Benedetti F, Grom AA, Brogan PA, et al. Efficacy and safety of emapalumab in macrophage activation syndrome. *Ann Rheum Dis*. 2023;82(6):857-865. doi:10.1136/ard-2022-223739
9. Fautrel B, Mitrovic S, De Matteis A, 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;83(12):1614-1627. Published 2024 Nov 14. doi:10.1136/ard-2024-225851
10. Shakoory B, Geerlinks A, Wilejto M, et al. The 2022 EULAR/ACR points to consider at the early stages of diagnosis and management of suspected haemophagocytic lymphohistiocytosis/macrophage activation syndrome (HLH/MAS). *Ann Rheum Dis*. 2023;82(10):1271-1285. doi:10.1136/ard-2023-224123

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