CareSource Rxinnovations

PHARMACY POLICY STATEMENT
Indiana 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) blocking 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.
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.

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) Body weight < 3 kg
   c) Active infection with mycobacteria, Histoplasma capsulatum, shigella, salmonella, campylobacter or leishmania
   d) Presence of malignancy; AND

6. Member must have a negative TB test within 12 months prior to starting therapy; AND
7. Member has received vaccines or prophylaxis for Herpes Zoster, Pneumocystis jiroveccii, and fungal infections.
8. **Dosage allowed/Quantity limit:** Start with 1 mg/kg as an intravenous infusion twice per week; may increase based on clinical response, up to a max of 10 mg/kg. See prescribing information for dose titration criteria.

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

For **reauthorization**:
1. Member has documented chart notes indicating ONE of the following:
   a) Complete response, defined as normalization of all HLH abnormalities (i.e., no fever, no splenomegaly, neutrophils > $1x10^9$ /L, platelets > $100x10^9$ /L, ferritin < 2,000 mg/L, fibrinogen > 1.50 g/L, D-dimer < 500 ug/L, normal CNS symptoms, no worsening of soluble CD25 > 2-fold baseline)
   b) Partial response, defined as normalization of ≥ 3 HLH abnormalities (see above)
   c) HLH improvement, defined as ≥ 3 HLH abnormalities improved by at least 50% from baseline; 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.

CareSource 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.

References:

1. Gamifant [prescribing information]. Waltham, MA: Sobi Inc.; 2022.
2. 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
3. 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
4. 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/
5. 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

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