Clinical Policy: Emapalumab-lzsg (Gamifant)

Reference Number: LA.PHAR.402
Effective Date: 10.05.23
Last Review Date: 03.05.25
Line of Business: Medicaid

Coding Implications
Revision Log

See Important Reminder at the end of this policy for important regulatory and legal information.

****Please note: This policy is for medical benefit****

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.

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 Louisiana Healthcare Connections 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 10^9 /L, neutrophils < 1 x 10^9/L);
      4) Hypertriglyceridemia (fasting TG ≥ 3 mmol/L or ≥ 265 mg/dL) and/or hypofibrinogenemia (fibrinogen ≤ 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 ≥ 500 mcg/L;
      8) Soluble CD25 (sCD25; i.e., soluble IL-2 receptor) ≥ 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. 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 LA.PMN.255
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 LA.PMN.53.

II. Continued Therapy

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

a. Currently receiving medication via Louisiana Healthcare Connections benefit or member has previously met initial approval criteria;
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. 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 LA.PMN.255
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 LA.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 – LA.PMN.53.

IV. Appendices/General Information

Appendix A: Abbreviation/Acronym Key
FDA: Food and Drug Administration
HLH: hemophagocytic lymphohistiocytosis
HSCT: hematopoietic stem cell transplantation

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®)	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	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

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 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.

- Gamifant is currently not indicated for the treatment of secondary HLH. Secondary HLH generally presents in adults and is triggered by autoimmune disease, infections, or cancer. Treatment for secondary HLH is focused on the triggering condition.

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

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; July 2024. Available at: https://www.gamifant.com/pdf/Full-Prescribing-Information.pdf. Accessed October 22, 2024.
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.

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	LDH Approval Date
Converted corporate to local policy	02.23	03.16.23
Updated criteria for other diagnoses/indications	06.25.23	10.05.23
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.	05.27.24	08.20.24
Annual review: no significant changes; added additional vial sizes per updated prescribing information; references reviewed and updated; references reviewed and updated.	03.05.25	

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. LHCC 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.

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 LHCC administrative policies and procedures.

This clinical policy is effective as of the date determined by LHCC. 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. LHCC 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 LHCC has no control or right of control. Providers are not agents or employees of LHCC.