Gamifant® (emapalumab-lzsg)
(Intravenous)

Document Number: IC-0421

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I. Length of Authorization

Coverage will be provided for 6 months and may be renewed.

II. Dosing Limits

A. Quantity Limit (max daily dose) [NDC Unit]:

- Gamifant 10 mg/2 mL single-dose vial: 32 vials per 30 days (4 vials per dose)
- Gamifant 50 mg/10 mL single-dose vial: 8 vials per 30 days (1 vial per dose)
- Gamifant 100 mg/20 mL single-dose vial: 88 vials per 30 days (11 vials per dose)

B. Max Units (per dose and over time) [HCPCS Unit]:

- 2300 billable units weekly

III. Initial Approval Criteria [1,3-7]

Coverage is provided in the following conditions:

Universal Criteria

- Patient has been evaluated and screened for the presence of latent tuberculosis (TB) infection prior to initiating treatment and will receive ongoing monitoring, every 2 weeks and as clinically indicated, for the presence of TB during treatment; **AND**
- Patient will receive prophylaxis for Herpes Zoster, *Pneumocystis Jirovecii*, and fungal infections; **AND**
- Patient does not have an active infection, including clinically important localized infections that are favored by interferon-gamma (e.g., infections caused by mycobacterium, histoplasma, etc.); **AND**
- Must not be administered concurrently with live or live attenuated vaccines; **AND**
- Patient has NOT received hematopoietic stem cell transplant (HSCT)*; **AND**

Hemophagocytic Lymphohistiocytosis (HLH) † Φ

- Patient has a definitive diagnosis of HLH as indicated by the following:

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- Patient diagnosis of primary HLH based on identification of biallelic pathogenic gene variants from molecular genetic testing (e.g., *PRF1, UNC13D, STX11, or STXBP2)* or a family history consistent with primary HLH; **OR**
- Patient has at least FIVE of the following eight documented criteria:
  - Prolonged fever (> 7 days)
  - Splenomegaly
  - Cytopenias affecting 2 of 3 lineages in the peripheral blood (hemoglobin < 9 g/dL, platelets < 100 x 10^9/L, neutrophils < 1 x 10^9/L)
  - Hypertriglyceridemia (fasting triglycerides > 3 mmol/L or ≥ 265 mg/dL) and/or hypofibrinogenemia (≤ 1.5 g/L)
  - Hemophagocytosis in bone marrow, spleen, or lymph nodes with no evidence of malignancy
  - Low or absent NK-cell activity
  - Ferritin ≥ 500 mcg/L
  - Soluble CD25 (aka soluble IL-2Rα receptor) ≥ 2400 U/mL; **AND**

- Patient has active, primary disease that is refractory, recurrent, or progressive during, or were intolerant of, conventional HLH therapy (e.g., dexamethasone, etoposide, cyclosporine A, anti-thymocyte globulin, etc.); **AND**
- Used in combination with dexamethasone (*Note: Patients currently on oral cyclosporine A, or intrathecal methotrexate and/or glucocorticoids may continue on therapy while treated with emapalumab)*

† FDA Approved Indication(s); ‡ Compendium Recommended Indication(s); Φ Orphan Drug

IV. Renewal Criteria [1,3-6]

Coverage can be renewed based on the following criteria:

- Patient continues to meet universal and other indication-specific relevant criteria such as concomitant therapy requirements (not including prerequisite therapy), etc. identified in section III; **AND**
- Absence of unacceptable toxicity from the drug. Examples of unacceptable toxicity include: serious infections (including mycobacteria, Herpes Zoster virus, and Histoplasma Capsulatum), infusion-related reactions (including drug eruption, pyrexia, rash, erythema, and hyperhidrosis), etc.; **AND**
- Patient is receiving ongoing monitoring every 2 weeks for adenovirus, EBV, and CMV viruses and as clinically indicated; **AND**
- Patient continues to require therapy for treatment of HLH; **AND**
- Patient experienced a disease improvement in HLH abnormalities as evidenced by one of the following:
  - 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 µg/L,*

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fibrinogen > 1.50 g/L, D-dimer < 500 µg/L, normal CNS symptoms, no worsening of sCD25 > 2-fold baseline); **OR**

- Partial response defined as normalization of ≥ 3 HLH abnormalities; **OR**
- HLH improvement defined as ≥ 3 HLH abnormalities improved by at least 50% from baseline; **OR**

- Dose escalation (up to the maximum dose and frequency specified below) requests based on clinical and laboratory parameters being interpreted as an unsatisfactory response are defined as at least ONE of the following:
  - Fever – persistence or recurrence
  - Platelet count
    - If baseline < 50,000/mm^3 and no improvement to >50,000/mm^3
    - If baseline > 50,000/mm^3 and less than 30% improvement
    - If baseline > 100,000/mm^3 and decrease to < 100,000/mm^3
  - Neutrophil count
    - If baseline < 500/mm^3 and no improvement to > 500/mm^3
    - If baseline > 500 -1000/mm^3 and decrease to < 500/mm^3
    - If baseline 1000-1500/mm^3 and decrease to < 1000/mm^3
  - Ferritin (ng/mL)
    - If baseline ≥ 3000 ng/mL and < 20% decrease
    - If baseline < 3000 ng/mL and any increase to > 3000 ng/mL
  - Splenomegaly – any worsening
  - Coagulopathy (both D-dimer and fibrinogen must apply)
    - D-Dimer
      - If abnormal at baseline and no improvement
    - Fibrinogen (mg/dL)
      - If baseline levels ≤ 100 mg/dL and no improvement
      - If baseline levels > 100 mg/dL and any decrease to < 100 mg/dL

**Patients should be evaluated for HSCT when a high-risk of relapse and a high-risk of mortality exists (e.g., homozygous or compound heterozygous HLH mutations exists, lack of response to initial HLH therapy, central nervous system involvement, and incurable hematologic malignancy).*

V. Dosage/Administration [1]

Indication	Dose
HLH	Administer initial doses of 1 mg/kg, intravenously over one hour, twice weekly. Titrate doses up to 10 mg/kg as follows: – On day 3, if an unsatisfactory improvement in clinical condition is assessed by the healthcare provider, increase to 3 mg/kg. – From day 6 and onwards, if an unsatisfactory improvement in clinical condition is assessed by the healthcare provider on the 3 mg/kg dose, increase to 6 mg/kg. – From day 9 and onwards, if an unsatisfactory improvement in clinical condition is assessed by the healthcare provider on the 6 mg/kg dose, increase to 10 mg/kg.
– Used in combination with dexamethasone at a daily dose of at least 5-10 mg/m^2 starting the day before Gamifant treatment begins. – Administer until hematopoietic stem cell transplantation (HSCT) is performed or unacceptable toxicity.	

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– Discontinue when a patient no longer requires therapy for the treatment of HLH.

VI. Billing Code/Availability Information

HCPCS Code:

- J9210 – Injection, emapalumab-lzsg, 1 mg; 1 billable unit = 1 mg

NDC:

- Gamifant 10 mg/2 mL single-dose vial: 66658-0501-xx
- Gamifant 50 mg/10 mL single-dose vial: 66658-0505-xx
- Gamifant 100 mg/20 mL single-dose vial: 66658-0510-xx

VII. References

1. Gamifant [package insert]. Waltham, MA; Sobi, Inc., May 2022. Accessed December 2022.
2. Jordan M, Locatelli F, Allen C, et al. A Novel Targeted Approach to the Treatment of Hemophagocytic Lymphohistiocytosis (HLH) with an Anti-Interferon Gamma (IFNγ) Monoclonal Antibody (mAb), NI-0501: First Results from a Pilot Phase 2 Study in Children with Primary HLH. Blood 2015 126:LBA-3
3. Zhang K, Astigarraga I, Bryceson Y, et al. Familial Hemophagocytic Lymphohistiocytosis. 2006 Mar 22 [Updated 2021 Sept 30]. In: Adam MP, Everman DB, Mirzaa GM, et al., editors. GeneReviews® [Internet]. Seattle (WA): University of Washington, Seattle; 1993-2022. Available from: https://www.ncbi.nlm.nih.gov/books/NBK1444/.
4. Jordan M, Allen C, Weitzman S, et al. How I treat hemophagocytic lymphohistiocytosis. Blood. 2011;118(15):4041. Epub 2011 Aug 9.
5. Ouachée-Chardin M, Elie C, de Saint Basile G, et al. Hematopoietic stem cell transplantation in hemophagocytic lymphohistiocytosis: a single-center report of 48 patients. Pediatrics. 2006;117(4):e743.
6. McClain KL. Treatment and prognosis of hemophagocytic lymphohistiocytosis. In Newburger P (Ed), *UpToDate*. Last updated: May 6, 2022. Accessed on December 1, 2022. Available from https://www.uptodate.com/contents/treatment-and-prognosis-of-hemophagocytic-lymphohistiocytosis?search=Treatment%20and%20prognosis%20of%20hemophagocytic%20lymphohistiocytosis&source=search_result&selectedTitle=1~150&usage_type=default&display_rank=1.
7. NovoImune SA. A Study to Investigate the Safety and Efficacy of an Anti-IFNγ mAb in Children Affected by Primary Haemophagocytic Lymphohistiocytosis. Available from: https://clinicaltrials.gov/ct2/show/NCT01818492?term=01818492&draw=1&rank=1. ClinicalTrials.gov Identifier: NCT01818492. Accessed December 2022.
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Appendix 1 – Covered Diagnosis Codes

ICD-10	ICD-10 Description
D76.1	Hemophagocytic lymphohistiocytosis

Appendix 2 – Centers for Medicare and Medicaid Services (CMS)

Medicare coverage for outpatient (Part B) drugs is outlined in the Medicare Benefit Policy Manual (Pub. 100-2), Chapter 15, §50 Drugs and Biologicals. In addition, National Coverage Determination (NCD), Local Coverage Articles (LCAs) and Local Coverage Determinations (LCDs) may exist and compliance with these policies is required where applicable. They can be found at: https://www.cms.gov/medicare-coverage-database/search.aspx. Additional indications may be covered at the discretion of the health plan.

Medicare Part B Covered Diagnosis Codes (applicable to existing NCD/LCA/LCD): N/A

Medicare Part B Administrative Contractor (MAC) Jurisdictions		
Jurisdiction	**Applicable State/US Territory**	**Contractor**
E (1)	CA, HI, NV, AS, GU, CNMI	Noridian Healthcare Solutions, LLC
F (2 & 3)	AK, WA, OR, ID, ND, SD, MT, WY, UT, AZ	Noridian Healthcare Solutions, LLC
5	KS, NE, IA, MO	Wisconsin Physicians Service Insurance Corp (WPS)
6	MN, WI, IL	National Government Services, Inc. (NGS)
H (4 & 7)	LA, AR, MS, TX, OK, CO, NM	Novitas Solutions, Inc.
8	MI, IN	Wisconsin Physicians Service Insurance Corp (WPS)
N (9)	FL, PR, VI	First Coast Service Options, Inc.
J (10)	TN, GA, AL	Palmetto GBA, LLC
M (11)	NC, SC, WV, VA (excluding below)	Palmetto GBA, LLC
L (12)	DE, MD, PA, NJ, DC (includes Arlington & Fairfax counties and the city of Alexandria in VA)	Novitas Solutions, Inc.
K (13 & 14)	NY, CT, MA, RI, VT, ME, NH	National Government Services, Inc. (NGS)
15	KY, OH	CGS Administrators, LLC

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Grievance Specialist
PreferredOne Community Health Plan
PO Box 59052
Minneapolis, MN 55459-0052
Phone: 1.800.940.5049 (TTY: 763.847.4013)
Fax: 763.847.4010
customerservice@preferredone.com

You can file a grievance in person or by mail, fax, or email. If you need help filing a grievance, a Grievance Specialist is available to help you.

You can also file a civil rights complaint with the U.S. Department of Health and Human Services, Office for Civil Rights, electronically through the Office for Civil Rights Complaint Portal, available at https://ocrportal.hhs.gov/ocr/portal/lobby.jsf, or by mail or phone at:

U.S. Department of Health and Human Services
200 Independence Avenue, SW
Room 509F, HHH Building
Washington, D.C. 20201
1-800-368-1019, 800-537-7697 (TDD)

Complaint forms are available at http://www.hhs.gov/ocr/office/file/index.html.

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PreferredOne Insurance Company
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Minneapolis, MN 55459-0212
Phone: 1.800.940.5049 (TTY: 763.847.4013)
Fax: 763.847.4010
customerservice@preferredone.com

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You can also file a civil rights complaint with the U.S. Department of Health and Human Services, Office for Civil Rights, electronically through the Office for Civil Rights Complaint Portal, available at https://ocrportal.hhs.gov/ocr/portal/lobby.jsf, or by mail or phone at:

U.S. Department of Health and Human Services
200 Independence Avenue, SW
Room 509F, HHH Building
Washington, D.C. 20201
1-800-368-1019, 800-537-7697 (TDD)

Complaint forms are available at http://www.hhs.gov/ocr/office/file/index.html.

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