Gamifant™ (emapalumab-lzsg)
(Intravenous)

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I. Length of Authorization

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

II. Dosing Limits

A. Quantity Limit (max daily dose) [Pharmacy Benefit]:

- 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: 184 vials per 30 days (23 vials per dose)

B. Max Units (per dose and over time) [Medical Benefit]:

- 2300 billable units weekly

III. Initial Approval Criteria

Coverage is provided in the following conditions:

- Patient has been evaluated and screened for the presence of latent TB infection prior to initiating 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 vaccines; **AND**

Hemophagocytic lymphohistiocytosis (HLH) †

- Patient has a definitive diagnosis of HLH as indicated by the following:
    - 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**
- Patient has NOT received hematopoietic stem cell transplant (HSCT)*; **AND**
- Used in combination with dexamethasone (*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)

IV. Renewal Criteria

Authorizations can be renewed based on the following criteria:

- Patient continues to meet the criteria identified in section III; **AND**
- Absence of unacceptable toxicity from the drug. Examples of unacceptable toxicity include the following: serious infections, severe infusion reactions, etc.; **AND**
- Patient is receiving ongoing monitoring for presence of TB or other active infections AND monitoring every 2 weeks for adenovirus, EBV, and CMV viruses and as clinically indicated; **AND**
- Patient has NOT received hematopoietic stem cell transplant (HSCT)*; **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, 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 any 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
            - 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

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 through 8, 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. – Discontinue when a patient no longer requires therapy for the treatment of HLH	

VI. Billing Code/Availability Information

HCPCS code:

- J3590 – Unclassified biologics
- J9210 – Injection, emapalumab-lzsg, 1 mg; 1 billable unit = 1 mg *(Effective 10/1/19)*

- C9050 – Injection, emapalumab-lzsg, 1 mg (Hospital Outpatient Use Only) - *effective 7/1/19*

NDC:

- Gamifant 10 mg/2 mL single-dose vial: 72171-0501-xx
- Gamifant 50 mg/10 mL single-dose vial: 72171-0505-xx

VII. References

1. Gamifant [package insert]. Waltham, MA; Sobi, Inc., November 2018. Accessed December 2018.
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, Filipovich AH, Johnson J, et al. Hemophagocytic Lymphohistiocytosis, Familial. 2006 Mar 22 [Updated 2013 Jan 17]. In: Adam MP, Ardinger HH, Pagon RA, et al., editors. GeneReviews® [Internet]. Seattle (WA): University of Washington, Seattle; 1993-2018. 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.

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) and Local Coverage Determinations (LCDs) may exist and compliance with these policies is required where applicable. They can be found at: http://www.cms.gov/medicare-coverage-database/search/advanced-search.aspx. Additional indications may be covered at the discretion of the health plan.

Medicare Part B Covered Diagnosis Codes (applicable to existing NCD/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

Medicare Part B Administrative Contractor (MAC) Jurisdictions		
Jurisdiction	**Applicable State/US Territory**	**Contractor**
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	Cahaba Government Benefit Administrators, 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