Emapalumab-lzsg (Gamifant™)

NDC CODE(S) 72171-0501-XX GAMIFANT 10MG/2ML Solution (SOBI)
72171-0505-XX GAMIFANT 50MG/10ML Solution (SOBI)
66658-0501-XX GAMIFANT 5MG/ML Solution (SOBI)
66658-0505-XX GAMIFANT 5MG/ML Solution (SOBI)
66658-0510-XX GAMIFANT 5MG/ML Solution (SOBI)

DESCRIPTION

Emapalumab-lzsg is an interferon gamma (IFNγ) blocking monoclonal antibody that binds to and neutralizes interferon gamma (IFNγ). Nonclinical data suggest that IFNγ plays a pivotal role in the pathogenesis of hemophagocytic lymphohistiocytosis (HLH) by being hypersecreted. Emapalumab-lzsg reduces the plasma concentrations of CXCL9, a chemokine induced by IFNγ. Emapalumab-lzsg is produced in Chinese Hamster Ovary cells by recombinant DNA technology.

POLICY

- Emapalumab-lzsg for the treatment of primary hemophagocytic lymphohistiocytosis (HLH) with refractory, recurrent or progressive disease or intolerance with conventional HLH therapy is considered ***medically necessary*** if the medical appropriateness criteria are met. **(See Medical Appropriateness below.)**

- Emapalumab-lzsg for the treatment of other conditions/diseases is considered ***investigational.***

MEDICAL APPROPRIATENESS

INITIAL APPROVAL CRITERIA

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 for 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)
- 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**
- 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)*

RENEWAL CRITERIA

- Patient continues to meet universal and other indication-specific relevant criteria such as concomitant therapy requirements (not including prerequisite therapy), etc. identified in initial approval criteria**; 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 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, 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).*

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	

LENGTH OF AUTHORIZATION

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

DOSAGE LIMITS

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

- 2300 billable units weekly

APPLICABLE TENNESSEE STATE MANDATE REQUIREMENTS

BlueCross BlueShield of Tennessee's Medical Policy complies with Tennessee Code Annotated Section 56-7-2352 regarding coverage of off-label indications of Food and Drug Administration (FDA) approved drugs when the off-label use is recognized in one of the statutorily recognized standard reference compendia or in the published peer-reviewed medical literature.

IMPORTANT REMINDER

We develop Medical Policies to provide guidance to Members and Providers. This Medical Policy relates only to the services or supplies described in it. The existence of a Medical Policy is not an authorization, certification, explanation of benefits or a contract for the service (or supply) that is referenced in the Medical Policy. For a determination of the benefits that a Member is entitled to receive under his or her health plan, the Member's health plan must be reviewed. If there is a conflict between the Medical Policy and a health plan, the express terms of the health plan will govern.

ADDITIONAL INFORMATION

For appropriate chemotherapy regimens, dosage information, contraindications, precautions, warnings, and monitoring information, please refer to one of the standard reference compendia (e.g., the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) published by the National Comprehensive Cancer Network®, Drugdex Evaluations of Micromedex Solutions at Truven Health, or The American Hospital Formulary Service Drug Information).

SOURCES

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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/
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6. McClain, KL. Treatment and prognosis of hemophagocytic lymphohistiocytosis. In: UpToDate, Newburger, P (Ed), UpToDate, Waltham, MA. Updated December 2018. Accessed December 2019.
7. NovoImune NA. A Phase 2/3, Open-label, Single Arm, Multicentre Study to Assess Safety, Tolerability, Pharmacokinetics and Efficacy of Intravenous Multiple Administrations of NI-0501, an Anti-interferon Gamma (Anti-IFNγ) Monoclonal Antibody, in Paediatric Patients With Primary Haemophagocytic Lymphohistiocytosis. Available from: https://clinicaltrials.gov/ct2/show/NCT01818492?term=01818492&draw=1&rank=1. ClinicalTrials.gov Identifier: NCT01818492. Accessed December 2019.
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9. MICROMEDEX Healthcare Series. Drugdex Evaluations. (2020, June). Emapalumab-lzsg. Retrieved January 21, 2021 from MICROMEDEX Healthcare Series.

EFFECTIVE DATE 6/2/2021

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