MetroPlus Health

Policy and Procedure

Title: UM-PT121 Gamifant (emapalumab-lzsg)	Division: Medical Management Department: Pharmacy
Approval Date: 4/30/2025	LOB: Medicaid, SNP, HARP, CHP, QHP, EP, Gold, Goldcare
Effective Date: 4/30/2025	Policy Number: UM-PT121
Review Date: 3/4/2026	Cross Reference Number:
Retired Date:	Page 1 of 11

I. POLICY DESCRIPTION:

Monoclonal Antibody - Gamifant (emapalumab-lzsg)

II. RESPONSIBLE PARTIES:

Medical Management Administration, Pharmacy Department, Utilization Management, Integrated Care Management, Claims Department

III. DEFINITIONS:

Gamifant is an interferon gamma (IFNγ) blocking antibody, it binds to and neutralizes interferon gamma (IFNγ). Once IFNγ is neutralized, it blocks its intracellular signaling to inhibit macrophage activation and the downstream release of proinflammatory cytokines.

Gamifant is indicated for the treatment of:

1. Adult and pediatric (newborn and older) patients with primary hemophagocytic lymphohistiocytosis (HLH) with refractory, recurrent or progressive disease or intolerance with conventional HLH therapy.
2. Adult and pediatric (newborn and older) patients with HLH/macrophage activation syndrome (MAS) in known or suspected Still's disease, including systemic Juvenile Idiopathic Arthritis (sJIA), with an inadequate response or intolerance to glucocorticoids, or with recurrent MAS.

IV. POLICY:

Gamifant will be considered medically necessary once the following coverage criteria is met. Approvals may be subject to dosing limits in accordance with FDA-approved labeling, accepted compendia, and/or evidence-based practice guidelines.

Chart notes must be submitted to confirm diagnosis and previous treatment(s).

INITIAL REQUEST:

1. Primary hemophagocytic lymphohistiocytosis (HLH)

A. Member has a diagnosis of primary hemophagocytic lymphohistiocytosis (HLH);
AND
B. Prescribed by or in consultation with a hematologist or oncologist;
AND
C. Member HLH diagnosis is confirmed based on ALL of the following:
- **a.** Mutation in ONE of the following genes:
  - **i.** FHL2-PRF1;
    OR
  - **ii.** FHL3-UNC13D;
    OR

iii. FHL4-STX1;
OR
iv. FHL5-STXBP2;
OR
v. Griscelli type 2- RAB27A;
OR
vi. Chediak-Higashi- LYST;
OR
vii. XLP1 Duncan disease- SH2D1A;
OR
viii. BIRC4;
OR
ix. XLP2- NLRC4;

AND

b. Presence of at least five of the following clinical signs and symptoms of HLH:
- **i.** Fever ≥ 38.5°C (or 101.3°F);
- **ii.** Splenomegaly;
- **iii.** Cytopenias affecting two of the following lineages in the peripheral blood:
  - **1.** Hemoglobin < 9 g/dL (or <10 g/dL in infants < 4 weeks of age);
  - **2.** Platelets < 100 x 10^9 /L;
  - **3.** Neutrophils < 1 x 10^9/L;
- **iv.** Hypertriglyceridemia defined as fasting trigylcerides ≥ 3 mmol/L or ≥ 265 mg/dL;
- **v.** Hypofibrinogenemia defined as fibrinogen ≤ 1.5g/L;
- **vi.** Hemophagocytosis in bone marrow, spleen, or lymph nodes with no evidence of malignancy;
- **vii.** Low or absent Natural Killer cell activity (according to local laboratory reference;
- **viii.** Ferritin ≥ 500 mcg/L;
- **ix.** Soluble CD25 (sCD25; i.e., soluble IL-2 receptor) defined as ≥ 2400 U/mL;

AND

D. Member has refractory, recurrent, or progressive disease and failed or had a contraindication to at least one conventional HLH therapy (i.e., corticosteroids, cyclosporine A (CSA), intrathecal therapy, etoposide);

AND

E. Member does not have ANY of the following:

a. Diagnosis of secondary Hemophagocytic Lymphohistiocytosis consequent to a proven rheumatic or neoplastic disease;

OR

b. Active Mycobacteria, Histoplasma Capsulatum, Shigella, Salmonella, Campylobacter and Leishmania infections;

OR

c. Evidence of past history of tuberculosis or of latent tuberculosis *(Note: Member should have testing for latent tuberculosis infections using the purified protein derivative (PPD) or IFNγ release assay. If member has a positive PPD test result, or positive IFNγ release assay then tuberculosis prophylaxis should be completed prior to initiation of Gamifant);*

OR

d. Positive serology for human immunodeficiency virus antibodies, hepatitis B surface antigen or hepatitis C antibodies;

OR

e. Presence of malignancy;

OR

f. Another concomitant disease or malformation severely affecting the cardiovascular, pulmonary, central nervous system (CNS), liver or renal function *(Note: If member has any of this then attestation needs to be provided which states that member is being followed by a qualified physician per condition to monitor member if Gamifant is still to be given per physician's discretion)*;

AND

F. Member's current body weight has been obtained within the past 30 days;

AND

G. Gamifant will be administered concurrently with dexamethasone;

AND

H. Gamifant will be used until hematopoietic stem cell transplantation (HSCT) is performed or unacceptable toxicity.

AND

I. Member will have or has prophylaxis administered for Herpes Zoster, Pneumocystis jirovecii, and for fungal infections prior to initiation of therapy with Gamifant;

AND

J. Member will not receive live vaccines during Gamifant therapy and for at least 4 weeks after the last dose of Gamifant;

AND

K. Member will be monitored for tuberculosis, adenovirus, Epstein–Barr virus (EBV) and Cytomegalovirus (CMV) as clinically indicated;

AND

L. Authorization is for no more than 8 weeks.

2. Macrophage Activation Syndrome (MAS) in known or suspected Still's Disease

A. Member has a diagnosis of active Macrophage Activation Syndrome (MAS) as confirmed by the following:

a. Fever ≥ 38.5°C (or 101.3°F);

AND

b. Ferritin levels > 684 ng/mL;

AND

c. TWO of the following:

i. Platelet count ≤ 181 x 10^9/L;

ii. AST levels > 48 U/L;

iii. Triglycerides > 156 mg/dL;

iv. Fibrinogen levels ≤ 360 mg/dL;

AND

B. Prescribed by or in consultation with a board-hematologist or oncologist;

AND

C. Member is diagnosed with Still's disease or suspected to have Still's disease including systemic Juvenile Idiopathic Arthritis (sJIA);

AND

D. Member must have an inadequate response to high dose IV glucocorticoid treatment (>2mg/kg/day of prednisolone equivalent in two divided doses) for at least 3 consecutive days;

AND

E. Member must have failed, had intolerance to, or have a documented contraindication to interleukin-1 pathway inhibition (e.g., anakinra), unless clinically inappropriate due to rapidly progressive or life-threatening disease.
AND

F. Member does not have ANY of the following:

a. Active Mycobacteria, Histoplasma Capsulatum, Shigella, Salmonella, Campylobacter and Leishmania infections;

OR

b. Evidence of past history of tuberculosis or of latent tuberculosis *(Note: Member should have testing for latent tuberculosis infections using the purified protein derivative (PPD) or IFNγ release assay. If member has a positive PPD test result, or positive IFNγ release assay then tuberculosis prophylaxis should be completed prior to initiation of Gamifant);*

OR

c. Presence of malignancy**;**

OR

d. Positive serology for human immunodeficiency virus antibodies, hepatitis B surface antigen or hepatitis C antibodies;

OR

e. Another concomitant disease or malformation severely affecting the cardiovascular, pulmonary, central nervous system (CNS), liver or renal function *(Note: If member has any of this then attestation needs to be provided which states that member is being followed by a qualified physician per condition to monitor member if Gamifant is still to be given per physician's discretion)*;

AND

G. Member's current body weight has been obtained within the past 30 days;

AND

H. Gamifant will be administered concurrently with dexamethasone;

AND

I. Member will have or has prophylaxis administered for Herpes Zoster, Pneumocystis jirovecii, and for fungal infections prior to initiation of therapy with Gamifant;

AND

J. Member will not receive live vaccines during Gamifant therapy and for at least 4 weeks after the last dose of Gamifant;

AND

K. Member will be monitored for tuberculosis, adenovirus, Epstein–Barr virus (EBV) and Cytomegalovirus (CMV) as clinically indicated;

AND

L. Authorization is for no more than 8 weeks.

3. Recurrent MAS in known or suspected Still's disease

A. Member meets all of the following criteria above that is relevant to MAS;
AND

B. Member has experienced at least two (2) distinct, documented MAS episodes within a 12-month period;
AND

C. Each prior episode required inpatient hospitalization and/or intravenous glucocorticoid therapy;
AND

D. Members who were not previously treated with Gamifant for the immediate preceding MAS episode will require ALL of the following documented clinical and laboratory resolutions prior to recurrence:

i. Resolution of fever;
AND

ii. Clinical stabilization;

AND

iii. Ferritin decreased below the MAS diagnostic threshold of 684 ng/mL;
AND

iv. Improvement in at least one additional MAS laboratory parameter;
AND

E. If the member previously received Gamifant, clinical documentation must demonstrate:

i. Objective clinical improvement during the prior episode;
AND

ii. Reduction in ferritin from baseline;
AND

iii. Discontinuation of Gamifant following resolution;
AND

F. The current request is for treatment of a NEW MAS episode meeting all above criteria;
AND

G. Gamifant is not being prescribed for chronic, maintenance, prophylactic, or steroid-sparing use;
AND

H. Authorization may not exceed 4 weeks per episode, and total treatment per episode may not exceed 8 weeks.

RENEWAL REQUEST:

1. Primary hemophagocytic lymphohistiocytosis (HLH)

A. Initial conditions of coverage have been met;
AND

B. Member has no evidence of unacceptable toxicity (i.e., unwarranted infections related to mycobacteria, Herpes Zoster virus, and Histoplasma Capsulatum; infusion related reactions) or disease progression while on the current regimen;
AND

C. Member experiences a disease improvement in HLH abnormalities as evidenced by ONE of the following:

a. Complete response defined as normalization of all HLH abnormalities (e.g, no fever, no splenomegaly, neutrophils > 1 x 10^9g/L, platelets > 100 x 10^9g/L, ferritin < 2000µg/L, fibrinogen > 1.50 g/L, D-dimer < 500 µg/L, normal CNS symptoms, no worsening of sCD25 > 2-fold baseline);
OR

b. Partial response defined as normalization of ≥ 3 HLH abnormalities (including CNS abnormalities);
OR

c. HLH improvement defined as improvement by at least 50% from baseline of ≥ 3 HLH clinical and laboratory criteria (including CNS involvement);

AND

D. Authorization is for no more than 8 weeks

2. Macrophage Activation Syndrome (MAS) in known or suspected Still's Disease

A. Initial conditions of coverage have been met;

AND

B. Member has no evidence of unacceptable toxicity (i.e., unwarranted infections related to mycobacteria, Herpes Zoster virus, and Histoplasma Capsulatum; infusion related reactions);

AND

C. Member experienced a complete response as defined by clinical resolution of MAS signs and symptoms (a visual analogue scale (VAS), of ≤ 1 cm and the following laboratory parameters:

a. WBC and platelet count above the lower limit of normal;

AND

b. Lactate dehydrogenase, AST, and ALT below 1.5 times the upper limit of normal;

AND

c. Fibrinogen > 100mg/dL;

AND

d. Ferritin levels decreased ≥ 80% from baseline or < 2000 ng/mL (whichever is lower);

AND

D. Authorization is for no more than 4 weeks.

3. Recurrent MAS in known or suspected disease:

A. Member must continue to meet all initial coverage criteria for recurrent MAS;

AND

B. Member must have no evidence of unacceptable toxicity, including but not limited to serious or uncontrolled infections (e.g., mycobacteria, invasive fungal infection, EBV, CMV, adenovirus);

AND

C. Member must not have experienced infusion-related reactions requiring permanent discontinuation of therapy;

AND

D. Member must demonstrate objective clinical improvement during the previous MAS episode, defined as ALL of the following:

i. Resolution of fever (temperature < 38.0° C for ≥ 24 hours);

AND

ii. Clinical stabilization without progressive organ dysfunction;
AND

iii. Ferritin decreased by ≥ 50% from peak value during the current episode OR decreased below 684 ng/mL;
AND

iv. Improvement in at least one additional MAS laboratory parameter (platelet count, AST, triglycerides, or fibrinogen);

AND

E. Member must not be receiving Gamifant for chronic, maintenance, prophylactic, or steroid-sparing purposes;
AND

F. Member must be receiving Gamifant solely for management of the current acute MAS episode;
AND

G. Total duration of Gamifant therapy per MAS episode must not exceed 8 weeks.

V. LIMITATIONS/ EXCLUSIONS:

Gamifant will be considered experimental and investigational if prescribed for indications that have not been approved by the FDA and will not be covered under this policy. Gamifant should not be used concurrently with other biologics or targeted immunomodulators for the same indication unless medically justified. Requests for doses or frequencies outside FDA-labeled dosing may be denied or reviewed only with compelling supporting documentation.

VI. APPLICABLE PROCEDURE CODES:

CPT	Description
J9210	Injection, emapalumab-lzsg, 1 mg

VII. APPLICABLE DIAGNOSIS CODES:

CODE	Description
D76.1	Hemophagocytic lymphohistiocytosis

VIII. REFERENCES:

1. Gamifant [package insert]. Stockholm, Sweden: Swedish Orphan Biovitrum AB; June 2025.
2. Gamifant. IBM Micromedex® DRUGDEX ® (electronic version). IBM Watson Health, Greenwood Village, Colorado, USA. Available at https://www.micromedexsolutions.com

3. Study to Investigate Safety, Efficacy of an Anti-IFNγ mAb in Children With Primary Haemophagocytic Lymphohistiocytosis- Full Text View - ClinicalTrials.gov. clinicaltrials.gov. ClinicalTrials.gov Identifier: NCT01818492. https://clinicaltrials.gov/study/NCT01818492#study-overview.
4. Jordan MB, Allen CE, Weitzman S, Filipovich AH, McClain KL. How I treat hemophagocytic lymphohistiocytosis. Blood. 2011;118(15):4041-4052.
5. IPD Analytics. New Drug Review.
6. IPD Analytics. ICD-10-CM CODES.
7. ClinicalTrials.gov. Study to Investigate the Safety and Efficacy of Emapalumab, an Anti-IFN-gamma mAb in Patients With Systemic Juvenile Idiopathic Arthritis or Adult-onset Still's Disease Developing MAS/sHLH. ClinicalTrials.gov Identifier: NCT03311854. Updated May 17, 2022. https://clinicaltrials.gov/study/NCT03311854
8. Sztajnbok F, Fonseca AR, Campos LR, et al. Hemophagocytic lymphohistiocytosis and macrophage activation syndrome: two rare sides of the same devastating coin. Adv Rheumatol. 2024;64:28. doi:10.1186/s42358-024-00370-2
9. Swedish Orphan Biovitrum. NCT03311854 Gamifant Protocol: A pilot, open-label, single arm, multicenter study to evaluate safety, tolerability, pharmacokinetics and efficacy of emapalumab in sJIA or AOSD patients developing MAS/sHLH. Version 2.0. January 7, 2020
10. ClinicalTrials.gov. Evaluate Efficacy, Safety and Tolerability, PK and PD of Emapalumab in Children and Adults With MAS in Still's or SLE (EMERALD). ClinicalTrials.gov Identifier: NCT05001737. Updated June 11, 2025. https://clinicaltrials.gov/study/NCT05001737

REVISION LOG:

REVISIONS	INITIAL	DATE
Creation date	AKC	4/30/2025
Update	JL	3/4/2026

Approved:	Date:	Approved:	Date:
Suzana Patel	3/12/26		03.12.2026
Suzana Patel, PharmD **Senior Director of Pharmacy**		**Sanjiv Shah, MD** **Chief Medical Officer**	

Medical Guideline Disclaimer:

 The treating physician or primary care provider must submit MetroPlus Health Plan clinical evidence that the patient meets the criteria for the treatment or surgical procedure. Without this documentation and information, Metroplus Health Plan will not be able to properly review the request for prior authorization. The clinical review criteria expressed in this policy reflects how MetroPlus Health Plan determines whether certain services or supplies are medically necessary. MetroPlus Health Plan established the clinical review criteria based upon a review of currently available clinical information(including clinical outcome studies in the peer-reviewed published medical literature, regulatory status of the technology, evidence-based guidelines of public health and health research agencies, evidence-based guidelines and positions of leading national health professional organizations, views of physicians practicing in relevant clinical areas, and other relevant factors). MetroPlus Health Plan expressly reserves the right to revise these conclusions as clinical information changes, and welcomes further relevant information. Each benefit program defines which services are covered. The conclusion that a particular service or supply is medically necessary does not constitute a representation or warranty that this service or supply is covered andor paid for by MetroPlus Health Plan, as some programs exclude coverage for services or supplies that MetroPlus Health Plan considers medically necessary. If there is a discrepancy between this guidelines and a member's benefits program, the benefits program will govern. In addition, coverage may be mandated by applicable legal requirements of a state, the Federal Government or the Centers for Medicare & Medicaid Services (CMS) for Medicare and Medicaid members. All coding and website links are accurate at time of publication.

MetroPlus HealthPlan has adopted the herein policy in providing management, administrative and other services to our members, related to health benefit plans offered by our organization.