EVH Clinical Guideline 5104.CC for Gamifant

Guideline Number: EVH_CG_5104.CC	Applicable Codes	
"Evolent" refers to Evolent Health LLC and Evolent Specialty Services, Inc. 		
Original Date: September 2025	**Last Revised Date:** June 2025	**Implementation Date:** October 2025

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STATEMENT

General Information

- *It is the policy of the Health Plan to maintain a prior authorization process that promotes appropriate utilization of specific drugs with potential for misuse or limited indications. This process involves a review using Food and Drug Administration (FDA) criteria to make a determination of Medical Necessity, and approval by the Medical Policy Committee.*

- *If the established criteria are not met, the request is referred to a Medical Director for review, if required for the plan and level of request.*

Purpose

The purpose of this guideline is to define the prior authorization process for Gamifant (emapalumab-lzsg).

Scope

This guideline applies to all practitioners who are involved in providing the requested drug. This guideline is specific to the Health Plan's medical benefit.

INITIAL REVIEW CRITERIA

The request must meet all of the criteria listed below.

- Must be prescribed by, or in consultation with, a board-certified geneticist, pediatric metabolic specialist, hematologist, or physician experienced in the management of hemophagocytic lymphohistiocytosis (HLH)
- Must have a diagnosis of primary HLH confirmed by ONE of the following:
    - Genetic testing results confirming a gene mutation known to cause HLH [e.g., FHL3 – UNC13D, FHL2 – PRF1, RAB27A, STXBP2 (UNC18B), STX11]

    OR

    - At least five (5) of the following diagnostic criteria:
        - Persistent fever
        - Splenomegaly
        - Cytopenia involving at least 2 cell lines (hemoglobin less than 9 g/dL or less than 10 g/dL in infants less than 4 weeks of age, absolute neutrophil count less than 1000/µL, platelets less than 100,000/µL)
        - Hypertriglyceridemia (fasting triglycerides 265mg/dL or greater) or hypofibrinogenemia (fibrinogen less than 1.5 g/L)
        - Hemophagocytosis in bone marrow, spleen, or lymph nodes with no evidence of

malignancy
    - Low or absent natural killer (NK)-cell activity
    - Serum ferritin greater than 500 mcg/L
    - Elevated soluble interleukin-2 (CD25) levels (greater than 2400 U/mL
- Must provide documentation of all the following baseline disease-specific markers and lab values, as applicable
    - Fever (baseline temperature/frequency)
    - Splenomegaly
    - Description of central nervous system symptoms
    - Complete Blood Count (CBC)
    - Fibrinogen and/or D-dimer level
    - Ferritin level
    - Soluble CD25 level
- Must have a negative tuberculosis skin test collected within the last 6 months
    - Example acceptable testing includes the Tuberculin PPD (purified protein derivative) test or Interferon-Gamma Release Assay (IGRA) whole-blood test [such as QuantiFERON®-TB Gold In-Tube test (QFT-GIT) or T-SPOT®.TB test (T-Spot)]
- Must have a trial of conventional HLH therapy with refractory symptoms, progression of disease while on therapy, recurrence of disease following therapy OR have an intolerance to all conventional therapy regimens
    - Example conventional therapies include etoposide, corticosteroids, cyclosporine, antithymocyte globulin, methotrexate
- Must have chart note documentation or an attestation from the provider of all the following:
    - The provider has ruled out malignancy, viral infection and rheumatic disorders as a potential primary cause of HLH
    - The member is eligible for stem cell transplant and has NOT received a hematopoietic stem cell transplant (HSCT)
    - The member will be monitored for tuberculosis, adenovirus, EBV and CMV every 2 weeks and as clinically indicated while on Gamifant
    - The member will be given prophylactic treatment against herpes zoster, Pneumocystis jirovecii and fungal infections prior to Gamifant administration
    - The member will receive dexamethasone concurrently with Gamifant

REAUTHORIZATION CRITERIA

All prior authorization renewals are reviewed on an annual basis to determine the Medical Necessity for continuation of therapy. The request must meet all of the criteria listed below.

- *For first reauthorization ONLY:* Must submit genetic testing results confirming HLH if ONE of the following is applicable:
  - Initial approval was granted based on meeting diagnostic criteria alone
  - Member is new to plan and currently on drug
- Must submit documentation showing the member has NOT received hematopoietic stem cell transplant (HSCT) AND continues to require therapy for treatment of HLH
- Must provide an updated treatment plan that includes one of the following:
  - Anticipated hematopoietic stem cell transplant (HSCT) date, OR
  - Clinical rationale for why HSCT is not appropriate for member currently
- Must submit chart note documentation showing improvement in disease-specific markers or lab values, such as:
  - Fever
  - Splenomegaly
  - Description of central nervous system symptoms
  - Complete Blood Count (CBC)
  - Fibrinogen and/or D-dimer level
  - Ferritin level
  - Soluble CD25 level
- Must have no evidence of intolerable adverse effects or drug toxicity (e.g., serious infections, severe infusion reactions)

APPROVAL DURATIONS

Initial Authorization	6 months
Reauthorization	Same as initial

CODING AND STANDARDS

Codes

Code	Brand	Description
J9210	Gamifant	Injection, emapalumab-izsg, 1mg

Applicable Lines of Business

☐	CHIP (Children's Health Insurance Program)
☐	Commercial
☐	Exchange/Marketplace
☒	Medicaid
☐	Medicare Advantage

POLICY HISTORY

Date	Summary
September 2025	• New Guideline

LEGAL AND COMPLIANCE

Guideline Approval

Committee

Reviewed / Approved by Evolent Administrative Services Medical Policy Committee

Disclaimer

Evolent Clinical Guidelines do not constitute medical advice. Treating health care professionals are solely responsible for diagnosis, treatment, and medical advice. Evolent uses Clinical Guidelines in accordance with its contractual obligations to provide utilization management. Coverage for services varies for individual members according to the terms of their health care coverage or government program. Individual members' health care coverage may not utilize some Evolent Clinical Guidelines. Evolent clinical guidelines contain guidance

that requires prior authorization and service limitations. A list of procedure codes, services or drugs may not be all inclusive and does not imply that a service or drug is a covered or non-covered service or drug. Evolent reserves the right to review and update this Clinical Guideline in its sole discretion. Notice of any changes shall be provided as required by applicable provider agreements and laws or regulations. Members should contact their Plan customer service representative for specific coverage information.

Evolent Clinical Guidelines are comprehensive and inclusive of various procedural applications for each service type. Our guidelines may be used to supplement Medicare criteria when such criteria is not fully established. When Medicare criteria is determined to not be fully established, we only reference the relevant portion of the *corresponding Evolent Clinical Guideline that is applicable to the specific service or item requested in order to determine medical necessity.*

REFERENCES

1. Gamifant (emapalumab-lzsg) [prescribing information]. Waltham, MA: Sobi Inc; July 2024.
2. La Rosee, P, McClain K. Treatment and prognosis of hemophagocytic lymphohistiocytosis. In: Newburger P. UpToDate. UpToDate; 2025. Accessed April 29, 2025. www.uptodate.com
3. Locatelli F, Jordan MB, Allen C, et al. Emapalumab in Children with Primary Hemophagocytic Lymphohistiocytosis. N Engl J Med 2020; 382:1811