MEDICAL COVERAGE POLICY SERVICE: Emapalumab (Gamifant®)	
Policy Number:	**254**
Effective Date:	**07/01/2025**
Last Review:	**06/09/2025**
Next Review:	**06/09/2026**

Important note: *Unless otherwise indicated, medical policies will apply to all lines of business. Medical necessity as defined by this policy does not ensure the benefit is covered. This medical policy does not replace existing federal or state rules and regulations for the applicable service or supply. In the absence of a controlling federal or state coverage mandate, benefits are ultimately determined by the terms of the applicable benefit plan documents. See the member plan specific benefit plan document for a complete description of plan benefits, exclusions, limitations, and conditions of coverage. In the event of a discrepancy, the plan document always supersedes the information in this policy.*

SERVICE: Emapalumab (Gamifant®)

PRIOR AUTHORIZATION: Required.

POLICY: Please review the plan's EOC (Evidence of Coverage) or Summary Plan Description (SPD) for details.

For Medicare plans, please refer to appropriate Medicare NCD (National Coverage Determination) or LCD (Local Coverage Determination). If there are no applicable NCD or LCD criteria, use the criteria set forth below.

For Medicaid plans, please confirm coverage as outlined in the Texas Medicaid Provider Procedures Manual | TMHP (TMPPM). Texas Mandate HB154 is applicable for Medicaid plans.

Baylor Scott & White Health Plan (BSWHP) may consider emapalumab-lzsg (Gamifant®) medically necessary when documentation is submitted showing ALL of the following criteria are met:

Universal criteria:

1. Member has a documented diagnosis of primary hemophagocytic lymphohistiocytosis (HLH) based on a molecular diagnosis (e.g., PRF1, UNC13D, STX11 and STXBP2) or presence of 5 out of the following 8 criteria:
    a. Fever
    b. Splenomegaly
    c. Cytopenias affecting 2 of 3 lineages in the peripheral blood: hemoglobin less than 9 g/dL, platelets less than 100,000/microliter, neutrophils less than 1,000/microliter
    d. Hypertriglyceridemia (fasting triglycerides greater than 3 mmol/L or greater than or equal to 265 mg/dL) and/or hypofibrinogenemia (less than or equal to 1.5 g/L)
    e. Hemophagocytosis in bone marrow, spleen, or lymph nodes with no evidence of malignancy
    f. Low or absent NK-cell activity
    g. Ferritin greater than or equal to 500 mcg/L
    h. Soluble CD25 greater than or equal to 2400 U/mL

    AND
2. Member has refractory, recurrent, or progressive disease or intolerance with conventional HLH therapy; **AND**
3. Emapalumab is prescribed by or in consultation with a specialist that has expertise in the treatment of HLH; **AND**

4. Dexamethasone will be administered concomitantly with emapalumab

Initial requests:
1. Member meets all universal criteria; **AND**
2. Member is a candidate for stem cell transplant; **AND**
3. Emapalumab is being used as part of the induction or maintenance phase of stem cell transplant, which is to be discontinued at the initiation of conditioning for stem cell transplant; **AND**
4. Member has been evaluated for tuberculosis (TB) risk factors and has undergone pretreatment screening for latent TB with PPD skin test or interferon gamma release assay; **AND**
5. If member has a positive test result or is at risk for TB, prophylactic treatment for TB has been initiated before starting therapy

Renewal requests:

1. Member meets all universal criteria; **AND**
2. Member has improvement or stabilization of disease; **AND**
3. Member has manageable or no side effects

Initial authorization duration – 8 weeks
Renewal authorization duration – 6 months

BSWHP considers emapalumab for the treatment of all other indications to be experimental and investigational because the effectiveness of this strategy has not been established.

All requests will be reviewed by a clinical pharmacist and medical director.

BACKGROUND:
Hemophagocytic lymphohistiocytosis (HLH) is a life-threatening hyperinflammatory syndrome characterized by overactivation of the immune system. The disorder is classified into primary and secondary HLH. Primary HLH (also known as familial HLH) is a hereditary disorder, whereas secondary HLH develops as a complication in settings such as infection, malignancy, autoimmune disease, post-allogeneic hematopoietic cell transplantation (HCT), and drug hypersensitivity. Primary HLH may be caused by mutations in any of several genes that provide instructions for making proteins that help destroy or deactivate lymphocytes that are no longer needed. Approximately 40 to 60 percent of cases of primary HLH are caused by mutations in the PRF1 or UNC13D genes.

The overactivation of the immune system in HLH causes fever and damages the liver and spleen. HLH also destroys blood-producing cells in the bone marrow; as a result, affected individuals have a reduction in red blood cells and platelets, which can lead to bruising and abnormal bleeding. HLH can also lead to abnormalities of the heart, kidneys, and other organs and tissues. Affected individuals also have an increased risk of developing cancers of blood-forming cells (leukemia and lymphoma).

Primary HLH usually presents in childhood as an acute illness with prolonged fever, cytopenias, hepatosplenomegaly, liver dysfunction, neurologic dysfunction (seizures, retinal hemorrhages, ataxia, altered consciousness, or coma), and bone marrow hemophagocytosis. More than 10% of patients with HLH die within 2 months of diagnosis due to bleeding in the visceral organs, opportunistic infection due to neutropenia, or multiple organ failure. Primary HLH occurs in approximately 1 in 50,000 individuals worldwide.

Current care options for HLH include systemic steroids (primarily dexamethasone) combined with other immunosuppressive therapies (cyclosporine A and etoposide). Allogeneic HCT is the only curative therapy for HLH and is undertaken as early in life as feasible in children with confirmed primary HLH.

Emapalumab (Gamifant) is an intravenously administered fully human monoclonal antibody that is a potent inhibitor of interferon-gamma, a cytokine secreted by cells of the immune system to help regulate immune functions. Emapalumab is indicated for the treatment of adult and pediatric (newborn and older) patients with primary hemophagocytic lymphohistiocytosis (HLH) with refractory, recurrent, or progressive disease, or intolerance to conventional HLH therapy.

The efficacy of emapalumab was evaluated in a multicenter, open-label, single-arm trial NI-0501-04 (NCT01818492) in 27 pediatric patients with suspected or confirmed primary HLH with either refractory, recurrent, or progressive disease during conventional HLH therapy or who were intolerant of conventional HLH therapy. Efficacy was based upon overall response rate (ORR) at the end of treatment, defined as achievement of either a complete or partial response or HLH improvement. Twenty-seven patients enrolled and received treatment in the study and twenty patients (74%) completed the study. The ORR was 17 (63%) with a 95% confidence interval of 0.42 – 0.81, p-value 0.013. Overall response by category is 7 (26%) complete reponse, 8 (30%) partial response, and 2 (7.4%) HLH improvement.

CODES:

Important note: *Due to the wide range of applicable diagnosis codes and potential changes to codes, an inclusive list may not be presented, but the following codes may apply. Inclusion of a code in this section does not guarantee that it will be reimbursed, and patient must meet the criteria set forth in the policy language.*

CPT Codes:	
HCPCS Codes:	J9210 - Injection, emapalumab-lzsg, 1 mg
ICD10 codes:	
ICD10 Not covered:	

POLICY HISTORY:

Status	Date	Action
New	07/25/2019	New policy
Updated	06/29/2020	Logo changed to include FC
Reviewed	07/30/2020	Added HCPCS code, renewal criteria, and authorization duration.
Reviewed	07/22/2021	No changes
Reviewed	07/28/2022	No changes
Updated	07/27/2023	Updated Medicare criteria
Updated	07/24/2024	Applied new format and layout, updated background information
Updated	06/09/2025	Added specialist requirement. Updated renewal authorization duration to 6 months. Updated formatting and separated out into universal, initial, and renewal sections. Updated ending note sections to align with CMS requirements and business entity changes.
Update	8/11/2025	Removed, Medicare NCD/LCD Interqual statement for clarity.

REFERENCES:

The following scientific references were utilized in the formulation of this medical policy. BSWHP will continue to review clinical evidence related to this policy and may modify it at a later date based upon the evolution of the published clinical evidence. Should additional scientific studies become available, and they are not included in the list, please forward the reference(s) to BSWHP so the information can be reviewed by the Medical Coverage Policy Committee (MCPC) and the Quality Improvement Committee (QIC) to determine if a modification of the policy is in order.

1. Gamifant (emapalumab-lzsg) [prescribing information]. Waltham, MA: Sobi Inc; May 2022.
2. MedlinePlus [Internet]. Bethesda (MD): National Library of Medicine (US); [updated 2014 Nov 1]. Familial hemophagocytic lymphohistiocytosis; [reviewed 2014 Nov 1; cited 2019 Jul 25]; [about 1 p.]. Available from: https://medlineplus.gov/genetics/condition/familial-hemophagocytic-lymphohistiocytosis/.
3. Morimoto A., Nakazawa Y., Ishii E.: Hemophagocytic lymphohistiocytosis: pathogenesis, diagnosis, and management. Pediatr. Int. 2016; 58: pp. 817-825. PubMed PMID: 27289085
4. Zhang K, Astigarraga I, Bryceson Y, et al. Familial Hemophagocytic Lymphohistiocytosis. 2006 Mar 22 [Updated 2021 Sep 30]. In: Adam MP, Feldman J, Mirzaa GM, et al., editors. GeneReviews® [Internet]. Seattle (WA): University of Washington, Seattle; 1993-2024. Available from: https://www.ncbi.nlm.nih.gov/books/NBK1444/

***Note**:*
Health Maintenance Organization (HMO) products are offered through Scott and White Health Plan dba Baylor Scott & White Health Plan, and Scott & White Care Plans dba Baylor Scott & White Care Plan. Insured PPO and EPO products are offered through Baylor Scott & White Insurance Company. Scott and White Health Plan dba Baylor Scott & White Health Plan serves as a third-party administrator for self-funded employer-sponsored plans. Baylor Scott & White Care Plan and Baylor Scott & White Insurance Company are wholly owned subsidiaries of Scott and White Health Plan. These companies are referred to collectively in this document as Baylor Scott & White Health Plan.

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RightCare STAR Medicaid is offered through Scott and White Health Plan in the Central Texas Medicaid Rural Service Area (MRSA); FirstCare STAR is offered through SHA LLC dba FirstCare Health Plans (FirstCare) in the Lubbock and West MRSAs; and FirstCare CHIP is offered through FirstCare in the Lubbock Service Area.