MEDICAL COVERAGE POLICY	
SERVICE: Emapalumab (Gamifant)	
Policy Number:	**254**
Effective Date:	**09/01/2020**
Last Review:	**07/30/2020**
Next Review Date:	**07/31/2021**

Important note:
Unless otherwise indicated, this policy will apply to all lines of business.
Even though this policy may indicate that a particular service or supply may be considered medically necessary and thus covered, this conclusion is not based upon the terms of your particular benefit plan. Each benefit plan contains its own specific provisions for coverage and exclusions. Not all benefits that are determined to be medically necessary will be covered benefits under the terms of your benefit plan. You need to consult the Evidence of Coverage (EOC) or Summary Plan Description (SPD) to determine if there are any exclusions or other benefit limitations applicable to this service or supply. If there is a discrepancy between this policy and your plan of benefits, the provisions of your benefits plan will govern. However, applicable state mandates will take precedence with respect to fully insured plans and self-funded non-ERISA (e.g., government, school boards, church) plans. Unless otherwise specifically excluded, Federal mandates will apply to all plans. With respect to Medicare-linked plan members, this policy will apply unless there are Medicare policies that provide differing coverage rules, in which case Medicare coverage rules supersede guidelines in this policy. Medicare-linked plan policies will only apply to benefits paid for under Medicare rules, and not to any other health benefit plan benefits. CMS's Coverage Issues Manual can be found on the CMS website. Similarly, for Medicaid-linked plans, the Texas Medicaid Provider Procedures Manual (TMPPM) supersedes coverage guidelines in this policy where applicable.

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PRIOR AUTHORIZATION: Required.

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

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

For Medicaid plans, please confirm coverage as outlined in the Texas Medicaid TMPPM.

SWHP/FirstCare may consider emapalumab-lzsg (Gamifant) medically necessary for the treatment of pediatric and adult members with primary hemophagocytic lymphohistiocytosis (HLH) who have met the following criteria:

- 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:
  1. Fever;
  2. Splenomegaly;
  3. 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;
  4. 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);
  5. Hemophagocytosis in bone marrow, spleen, or lymph nodes with no evidence of malignancy;
  6. Low or absent NK-cell activity;
  7. Ferritin greater than or equal to 500 mcg/L;
  8. Soluble CD25 greater than or equal to 2400 U/mL; AND

- Member has refractory, recurrent, or progressive disease or intolerance with conventional HLH therapy; AND
- Member is a candidate for stem cell transplant; ANDEmapalumab 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
- 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
- If member has a positive test result or is at risk for TB, prophylactic treatment for TB has been initiated before starting therapy; AND
- Dexamethasone will be administered concomitantly with emapalumab.
- Authorization renewal requires clinical documentation submitted showing:
  1. Continued use of the drug and dosing is consistent with criteria above
  2. Improvement or stabilization of disease
  3. Manageable or no side effects

SWHP/FirstCare considers emapalumab experimental and investigational for all other indications.

Initial authorization approval duration is 8 weeks. Authorization renewal approval duration is 1 year.

OVERVIEW:

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.

SUPPORTING DATA:

CODES:

Important note:

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

CMS:

POLICY HISTORY:

Status	Date	Action
New	07/25/2019	New policy
	06/29/2020	Logo changed to include FC
Reviewed	07/30/2020	Added HCPCS code, renewal criteria, and authorization duration.

REFERENCES:

The following scientific references were utilized in the formulation of this medical policy. SWHP 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 SWHP 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. FDA label for Gamifant: https://gamifant.com/pdf/Full-Prescribing-Information.pdf