Emapalumab-lzsg (Gamifant™)

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 or government program (e.g., TennCare), the express terms of the health plan or government program will govern.

POLICY

INDICATIONS

The indications below including FDA-approved indications and compendial uses are considered a covered benefit provided that all the approval criteria are met and the member has no exclusions to the prescribed therapy.

FDA-Approved Indications

Gamifant 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 with conventional HLH therapy.
- 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.

All other indications are considered experimental/investigational and not medically necessary.

DOCUMENTATION

Submission of the following information is necessary to initiate the prior authorization review:
For initial requests chart notes, medical records, or claims history documenting:

- Primary hemophagocytic lymphohistiocytosis (HLH):
  - Previous medications tried, including response to therapy.
  - Confirmation of the diagnosis of HLH with the presence of one of the following: A) a mutation in one of the following genes: PRF1, UNC13D, STX11 and STXBP2, or B) presence of at least 5 clinical signs and symptoms of disease (see Appendix A).
- Macrophage activation syndrome (MAS) in known or suspected Still's disease:
  - Confirmed or suspected diagnosis of systemic Juvenile Idiopathic Arthritis (sJIA) or Adult-onset Still's disease (AOSD).
  - Confirmed diagnosis of active MAS.
  - Previous use of IV high-dose glucocorticoids, including response to therapy.

For continuation requests:

- Chart notes or medical record documentation supporting positive clinical response.

COVERAGE CRITERIA

Primary Hemophagocytic Lymphohistiocytosis (HLH)

Authorization of 6 months may be granted for treatment of primary hemophagocytic lymphohistiocytosis (HLH) when all of the following criteria are met:

- Member has refractory, recurrent or progressive disease or intolerance with conventional HLH therapy (e.g., etoposide, dexamethasone, cyclosporine, antithymocyte globulin).
- Member's diagnosis of primary HLH was confirmed by either of the following:
  - Mutation in one of the following genes: PRF1, UNC13D, STX11 and STXBP2.
  - Presence of at least 5 clinical signs and symptoms of HLH (see Appendix A).
- Possible causes of secondary or acquired forms of HLH (e.g., autoimmune disease, persistent infection, malignancy, or loss of inhibitory immune mechanisms) have been ruled out.
- Member has been evaluated for tuberculosis (TB) risk factors and has undergone pretreatment screening for latent TB with the purified protein derivative (PPD) skin test or interferon gamma release assay.
- If member has a positive test result or is at risk for TB, prophylactic treatment for TB must be initiated before starting therapy.

Macrophage Activation Syndrome (MAS) in Known or Suspected Still's Disease

Authorization of 6 months may be granted for treatment of macrophage activation syndrome (MAS) in known or suspected Still's disease when all of the following criteria are met:

- Member has a confirmed or suspected diagnosis of systemic Juvenile Idiopathic Arthritis (sJIA) or Adult-onset Still's disease (AOSD) (see Appendix B and C for clinical features associated with sJIA and AOSD).
- Member has a confirmed diagnosis of active MAS (e.g., persistent fever, elevated and/or rising ferritin or other markers of inflammation/damage, cytopenias, hepatic dysfunction, coagulopathy, splenomegaly, CNS dysfunction).
- Member has a documented inadequate response or intolerance to high-dose IV glucocorticoids (e.g., prednisolone given as 30 mg/kg pulses over 3 consecutive days).
- Primary hemophagocytic lymphohistiocytosis (HLH), active infections, and malignancy have been evaluated for and ruled out.
- Member has been evaluated for tuberculosis (TB) risk factors and has undergone pretreatment screening for latent TB with the purified protein derivative (PPD) skin test or interferon gamma release assay.
- If member has a positive test result or is at risk for TB, prophylactic treatment for TB must be initiated before starting therapy.

CONTINUATION OF THERAPY

Authorization of 12 months may be granted for continued treatment in members requesting reauthorization for primary hemophagocytic lymphohistiocytosis (HLH) or macrophage activation syndrome (MAS) who have achieved or maintained positive clinical response (e.g., improvement in any of the clinical or laboratory parameters used to demonstrate evidence of active disease on initial authorization).

APPENDICES

Appendix A: CLINICAL SIGNS AND SYMPTOMS OF HEMOPHAGOCYTIC LYMPHOHISTIOCYTOSIS (HLH)

- Fever
- Splenomegaly
- Cytopenias (affecting at least 2 of 3 lineages in the peripheral blood: hemoglobin less than 9 g/dL [hemoglobin less than 10 g/dL in infants younger than 4 weeks], platelets less than 100,000/microliter, neutrophils less than 1,000/microliter)
- Hypertriglyceridemia (fasting triglyceride greater than or equal to 265 mg/dL) or hypofibrinogenemia (less than or equal to 150 mg/dL)

- Hemophagocytosis in bone marrow or spleen or lymph nodes or liver with no evidence of malignancy
- Low or absent natural killer (NK) cell activity
- Ferritin greater than or equal to 500 ng/mL
- Soluble CD25 (soluble IL-2 receptor alpha) level greater than or equal to 2400 U/mL, or above age-adjusted, laboratory-specific normal levels (defined as 2 standard deviation from the mean)

Appendix B: Operational Case Definition of New Onset systemic Juvenile Idiopathic Arthritis

- Patient should have:
  - Age 6 months to 18 years
  - Fever for at least 2 weeks
  - Arthritis in one or more joints (6 weeks duration not required)
  - At least one of the following:
    - Evanescent erythematous rash
    - Generalized lymphadenopathy
    - Hepatomegaly or splenomegaly
    - Pericarditis, pleuritis and/or peritonitis
- Patient should not have any of the following:
  - Infection: including concomitant active or recurrent chronic bacterial, fungal or viral infection at presentation; nor underlying infection which may mimic initial presentation of sJIA
  - Malignancy
  - Positive screening test for TB without documented past treatment
  - Prior treatment for SJIA other than NSAIDs or short term steroids
  - Immunization with live virus vaccines within the 4 weeks prior to enrollment

Appendix C: Yamaguchi Diagnostic Criteria for Adult-onset Still's Disease

- Major Criteria
  - Fever ≥ 39 degrees Celsius persisting for ≥ 1 week
  - Arthralgia/arthritis persisting for greater than or equal to 2 weeks
  - Typical rash
  - White blood cell count greater than or equal to 10×10^9/L (> 80% neutrophils)
- Minor Criteria
  - Sore throat
  - Lymphadenopathy and/or splenomegaly
  - Increased serum aminotransferase or lactate dehydrogenase levels (after other causes have been excluded)
  - Negative IgM rheumatoid factor and antinuclear antibodies (immunofluorescence assay)
- Exclusion Criteria
  - Infections, in particular sepsis and infectious mononucleosis
  - Malignancy, in particular lymphoma
  - Other rheumatic diseases, in particular polyarteritis nodosa and vasculitis in the course of rheumatoid arthritis

For the diagnosis of Adult-onset Still's disease, ≥ 5 criteria must be met, including ≥ 2 major. In members with any of the exclusion criteria, the diagnosis is excluded.

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.

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).

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EFFECTIVE DATE 1/30/2026

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