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DRUG POLICY

Gamifant (emapalumab-lzsg)

NOTICE

This policy contains information which is clinical in nature. The policy is not medical advice. The information in this policy is used by Wellmark to make determinations whether medical treatment is covered under the terms of a Wellmark member's health benefit plan. Physicians and other health care providers are responsible for medical advice and treatment. If you have specific health care needs, you should consult an appropriate health care professional. If you would like to request an accessible version of this document, please contact customer service at 800-524-9242.

BENEFIT APPLICATION

Benefit determinations are based on the applicable contract language in effect at the time the services were rendered. Exclusions, limitations or exceptions may apply. Benefits may vary based on contract, and individual member benefits must be verified. Wellmark determines medical necessity only if the benefit exists and no contract exclusions are applicable. This medical policy may not apply to FEP. Benefits are determined by the Federal Employee Program.

DESCRIPTION

The intent of the policy is to provide coverage consistent with product labeling, FDA guidance, standards of medical practice, evidence-based drug information, and/or published guidelines. The indications below including FDA-approved indications and compendial uses are considered covered benefits 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:

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.

POLICY

Required Documentation

The following information is necessary to initiate the prior authorization review:

Primary hemophagocytic lymphohistiocytosis (HLH)

1. Initial requests include chart notes, medical records, or claims history documenting:
 - A. Previous medications tried, including response to therapy.
 - B. Confirmation of the diagnosis of HLH with the presence of one of the following:
 - 1) A mutation in one of the following genes: PRF1, UNC13D, STX11 and STXBP2

- 2) Presence of at least 5 clinical signs and symptoms of disease. (See Appendix A)
2. Continuation requests include chart notes or medical records supporting positive clinical response

Macrophage activation syndrome (MAS) in known or suspected Still's disease

1. Initial requests include chart notes, medical records, or claims history documenting:
 - A. Confirmed or suspected diagnosis of systemic Juvenile Idiopathic Arthritis (sJIA) or Adult-onset Still's disease (AOSD)
 - B. Confirmed diagnosis of active MAS
 - C. Previous use of IV high-dose glucocorticoids, including response to therapy
2. Continuation requests include chart notes or medical records supporting positive clinical response

Criteria for Initial Approval

Primary Hemophagocytic Lymphohistiocytosis (HLH)

Authorization of 6 months may be granted for treatment of primary HLH when ALL of the following criteria are met:

1. Member has refractory, recurrent or progressive disease or intolerance with conventional HLH therapy (e.g., etoposide, dexamethasone, cyclosporine, antithymocyte globulin)
2. Member's diagnosis of primary HLH was confirmed by either of the following:
 - A. Mutation in one of the following genes: PRF1, UNC13D, STX11 and STXBP2
 - B. Presence of at least 5 clinical signs and symptoms of HLH (See Appendix A)
3. 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
4. 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
5. 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:

1. 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)
2. 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)
3. Member has a documented inadequate response or intolerance to high-dose IV glucocorticoids (e.g., methylprednisolone given as 30 mg/kg pulses over 3 consecutive days)
4. Primary hemophagocytic lymphohistiocytosis (HLH), active infections, and malignancy have been evaluated for and ruled out
5. 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
6. 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).

Other

Gamifant (emapalumab-lzsg) is considered **not medically necessary** for members who do not meet the criteria set forth above.

Dosing and Administration

Approvals may be subject to dosing limits in accordance with FDA-approved labeling, accepted compendia, and/or evidence-based practice guidelines.

APPENDIX

Appendix A: Clinical Signs and Symptoms of Hemophagocytic Lymphohistiocytosis (HLH)

1. Fever
2. Splenomegaly
3. 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)
4. Hypertriglyceridemia (fasting triglyceride greater than or equal to 265 mg/dL) or hypofibrinogenemia (less than or equal to 150 mg/dL)
5. Hemophagocytosis in bone marrow or spleen or lymph nodes or liver with no evidence of malignancy
6. Low or absent natural killer (NK) cell activity
7. Ferritin greater than or equal to 500 ng/mL
8. 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

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

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

1. Major Criteria
 - A. Fever ≥ 39 degrees Celsius persisting for ≥ 1 week
 - B. Arthralgia/arthritis persisting for greater than or equal to 2 weeks

- C. Typical rash
- D. White blood cell count greater than or equal to $10 \times 10^9/L$ (>80% neutrophils)
- 2. Minor Criteria
 - A. Sore throat
 - B. Lymphadenopathy and/or splenomegaly
 - C. Increased serum aminotransferase or lactate dehydrogenase levels (after other causes have been excluded)
 - D. Negative IgM rheumatoid factor and antinuclear antibodies (immunofluorescence assay)
- 3. Exclusion Criteria
 - A. Infections, in particular sepsis and infectious mononucleosis
 - B. Malignancy, in particular lymphoma
 - C. 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.

PROCEDURES AND BILLING CODES

To report provider services, use appropriate CPT* codes, Alpha Numeric (HCPCS level 2) codes, Revenue codes, and/or ICD diagnostic codes.

- J9210: Injection, emapalumab-lzsg, 1 mg

REFERENCES

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POLICY HISTORY

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