Medical Coverage Policy | Gamifant™ (emapalumab-lzsg)

EFFECTIVE DATE: 10|01|2019
POLICY LAST UPDATED: 06|04|2019

OVERVIEW

Gamifant™ (emapalumab-lzsg) 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.

This policy is applicable to BlueCHiP for Medicare products only. For Commercial Products, see related policy section.

MEDICAL CRITERIA

Initial Evaluation

Gamifant™ (emapalumab-lzsg) will be approved when ALL of the following are met:

1. Work up for the diagnosis of primary hemophagocytic lymphohistiocytosis (HLH) was started prior to initiating therapy

AND

2. The patient's primary HLH is refractory to a conventional therapy regimen (e.g. includes immunosuppressive or pro-apoptotic chemotherapy [e.g. etoposide, corticosteroids, cyclophosphamide, cyclosporine, anti-thymocyte globulin, methotrexate])

AND

3. The patient is receiving concomitant dexamethasone therapy

AND

4. The prescriber is a specialist in the area of the patient's diagnosis (e.g. hematologist) or the prescriber has consulted with a specialist in the area of the patient's diagnosis

AND

5. The patient does NOT have any FDA labeled contraindications to the requested agent

AND

6. The requested dose is within FDA labeling

Length of Approval: 12 months

Renewal Evaluation

Gamifant™ (emapalumab-lzsg) will be approved when ALL of the following are met:

1. The patient has been previously approved for the requested agent through the Medical Drug Criteria approval process

AND

2. The patient has had clinical benefit with the requested agent

AND

3. The patient is receiving concomitant dexamethasone therapy

AND

4. The prescriber is a specialist in the area of the patient's diagnosis (e.g. hematologist) or the prescriber has consulted with a specialist in the area of the patient's diagnosis

AND

5. The patient does NOT have any FDA labeled contraindications to the requested agent

AND

6. The requested dose is within FDA labeling

Length of Approval: 12 months

PRIOR AUTHORIZATION
Prior authorization is required for BlueCHiP for Medicare.

POLICY STATEMENT
BlueCHiP for Medicare
Gamifant™ (emapalumab-lzsg) is medically necessary when the criteria above have been met.

COVERAGE
Benefits may vary between groups and contracts. Please refer to the appropriate Benefit Booklet, Evidence of Coverage or Subscriber Agreement for applicable physician administered drug benefits/coverage.

BACKGROUND
Hemophagocytic lymphohistiocytosis is an aggressive and life-threatening syndrome of excessive immune activation. Survival is dramatically increased with therapy and therapy should not be delayed due to specialized testing. Treatment may be begun on high clinical suspicion of diagnosis.

Historically, for clinical trials, diagnosis of primary HLH were confirmed through genetic testing or through confirmation of at least 5 of the following 8 findings:

- Fever ≥38.5°C
- Splenomegaly
- Peripheral blood cytopenia, with at least two of the following:
  - hemoglobin <9 g/dL (for infants <4 weeks, hemoglobin <10 g/dL)
  - platelets <100,000/microL
  - absolute neutrophil count <1000/microL
- Hypertriglyceridemia (fasting triglycerides >265 mg/dL) and/or hypofibrinogenemia (fibrinogen <150 mg/dL)
- Hemophagocytosis in bone marrow, spleen, lymph node, or liver
- Low or absent NK cell activity
- Ferritin >500 ng/mL (the author prefers to consider a ferritin >3000 ng/mL as more indicative of HLH)
- Elevated soluble CD25 (soluble IL-2 receptor alpha [sIL-2R]) two standard deviations above age-adjusted laboratory-specific norms

UptoDate also lists the following as options to consider for diagnosing HLH:

- A patient with abnormality in 1 of the 4 immune markers (hemophagocytosis, increased ferritin, hypofibrinogenemia, absent or very decreased NK cell function) AND 3 of the 4 clinical findings (fever, splenomegaly, cytopenias, hepatitis)
- A patient with CNS symptoms, cytopenias, fever, and ferritin over 3000 ng/mL or rapidly rising ferritin or elevated sCD25
- A patient with CNS symptoms, hepatitis, coagulopathy, and ferritin over 3000 ng/mL or rapidly rising ferritin or elevated sCD25
- A patient with hypotension, fever, no response to broad spectrum antibiotics, and ferritin over 3000 ng/mL or rapidly rising ferritin or elevated sCD25

A scoring system has also been developed to predict the probability of HLH. A score of ≥250 implies a 99% probability of HLH.

Conventional therapy for HLH include immunosuppressive and pro-apoptotic chemotherapy (etoposide, corticosteroids, cyclophosphamide, cyclosporine, anti-thymocyte globulin, and methotrexate). Hematopoietic cell transplantation (HCT) is the curative therapy for HLH.

Emapalumab was studied in a multicenter, open-label, single arm trial of 27 pediatric patients with suspected or confirmed primary hemophagocytic lymphohistiocytosis (HLH). Patients' HLH were either refractory, recurrent, or progressive disease while on conventional HLH therapy or the patient was intolerant of conventional HLH therapy. The median duration of treatment with emapalumab was 59 days. Patients were required to fulfill the following criteria for enrollment:

1. Primary HLH based on a molecular diagnosis or family history consistent with primary HLH or through confirmation of 5 of the 8 clinical findings described above.
2. Patients had to have evidence of active disease as assessed by treating physician.
3. Patients had to fulfill one of the following criteria as assessed by the treating physician:
    a. having not responded or not achieved a satisfactory response or not maintained a satisfactory response to conventional HLH therapy
        i. Prior therapies in the trial included the following agents: dexamethasone, etoposide, cyclosporine A, and anti-thymocyte globulin
    b. Intolerance to conventional HLH treatments.

For patients who are not receiving baseline dexamethasone treatment, begin dexamethasone at a daily dose of at least 5 to 10 mg/m2 the day before emapalumab treatment begins. For patients who were receiving baseline dexamethasone, they may continue their regular dose provided the dose is at least 5 mg/m2. Dexamethasone can be tapered according to the judgment of the treating physician.

CODING

BlueCHiP for Medicare

The following HCPCS code is covered when the medical criteria have been met:

C9050 Injection, emapalumab-lzsg, 1 mg

RELATED POLICIES

Prior Authorization of Drugs

PUBLISHED

Provider Update, August 2019

REFERENCES

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2. Clinical features and diagnosis of hemophagocytic lymphohistiocytosis. UptoDate. Current through 2/2019. Last updated 10/29/2018.
3. Jordan MB, Allen CE, Weitzman S, et al. How I treat hemophagocytic lymphohistiocytosis. Blood. 2011;118(15):4041. Epub 2011 Aug 9.
4. Bergsten E, Horne A, Aricó M, et al. Confirmed efficacy of etoposide and dexamethasone in HLH treatment: long-term results of the cooperative HLH-2004 study. Blood. 2017;130(25):2728. Epub 2017 Sep 21.
5. Wetizman S. Approach to hemophagoctic syndrome. Hematology. 2011. Available at https://www.histio.org/document.doc?id=295.
6. Fardet L, Galicier L, Lambotte O, et al. Development and validation of the HScore, a score for the diagnosis of reactive hemophagocytic syndrome. Arthritis and Rheumatology. 2014 Sep;66(9):2613-20.

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