Gamifant® (Emapalumab-Lzsg) (for Louisiana Only)

Policy Number: CSLA2023D0077G
Effective Date: December 1, 2023

Instructions for Use

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Application

This Medical Benefit Drug Policy only applies to the state of Louisiana.

Coverage Rationale

Emapalumab is proven and medically necessary for the treatment of primary hemophagocytic lymphohistiocytosis (HLH) in patients who meet all of the following criteria:[1-4]

- Submission of medical records (e.g., chart notes, laboratory values) confirming **one** the following:
  - Confirmation of a gene mutation known to cause primary HLH (e.g., PRF1, UNC13D); **or**
  - Confirmation that **five** of the following clinical characteristics are present:
    - Fever ≥ 101.3°F
    - Splenomegaly
    - **Two** of the following cytopenias in the peripheral blood:
      - Hemoglobin < 9 g/dL; **or**
      - Platelet count < 100 x 10^9/L; **or**
      - Neutrophils < 1 x 10^9/L
    - **One** of the following:
      - Hypertriglyceridemia defined as fasting triglycerides ≥ 3 mmol/L or ≥ 265 mg/dL; **or**
      - Hypofibrinogenemia defined as fibrinogen ≤ 1.5 g/L
    - Hemophagocytosis in bone marrow, spleen or lymph nodes with no evidence of malignancy
    - Low or absent natural killer cell activity (according to local laboratory reference)
    - Ferritin ≥ 500 mg/L
    - Soluble CD25 (i.e., soluble IL-2 receptor) ≥ 2,400 U/ml

  and
- Patient has refractory, recurrent or progressive disease or intolerance with conventional HLH therapy (i.e., etoposide + dexamethasone); **and**
- Emapalumab will be administered with dexamethasone; **and**
- Patient is a candidate for stem cell transplant; **and**

- 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**
- Dosing is in accordance with the United States Food and Drug Administration approved labeling; **and**
- Approval is for no more than 6 months

Emapalumab is not proven or medically necessary for the treatment of secondary HLH.

Applicable Codes

The following list(s) of procedure and/or diagnosis codes is provided for reference purposes only and may not be all inclusive. Listing of a code in this policy does not imply that the service described by the code is a covered or non-covered health service. Benefit coverage for health services is determined by federal, state, or contractual requirements and applicable laws that may require coverage for a specific service. The inclusion of a code does not imply any right to reimbursement or guarantee claim payment. Other Policies and Guidelines may apply.

HCPCS Code	Description
J9210	Injection, emapalumab-lzsg, 1 mg

Diagnosis Code	Description
D76.1	Hemophagocytic lymphohistiocytosis

Background

Emapalumab is a monoclonal antibody that binds to interferon gamma (IFN$_\gamma$) and neutralizes it. Nonclinical data suggest that IFN$_\gamma$ is involved in HLH by being hypersecreted. Emapalumab decreases plasma concentrations of CXCL9, a chemokine induced by IFN$_\gamma$.

Clinical Evidence

The efficacy of emapalumab in the treatment of HLH was assessed in study NI-0501-04, a phase 2-3, multicenter, single-arm clinical trial. The study was designed to study the pharmacokinetics, efficacy, and safety of emapalumab in pediatric patients with suspected or confirmed primary HLH who were treatment naive or had not responded to or were intolerant to standard HLH therapy. In the study, patients were treated for up to 8 weeks, but not less than 4 weeks based on patient condition and donor availability for hematopoietic stem cell transplantation. Initially, emapalumab was dosed 1mg/kg every three days until day 15, when it was administered twice weekly thereafter. Dose increases were allowed, up to 10mg/kg/day and dexamethasone was administered to study patients as well. The primary efficacy endpoint was overall response at the end of treatment, defined as achievement of either a complete or partial response or HLH improvement using protocol-specified criteria. Secondary efficacy endpoints included measures of the sustained control of HLH disease so that patients could receive hematopoietic stem cell transplantation as well as survival. Overall, 64.7% of study patients had an overall response at end of treatment. Overall, 88.2% of patients responded to emapalumab treatment, with disease control occurring shortly after initiation of emapalumab treatment, with a median time to first response of 8 days. Overall, 65% of patients underwent hematopoietic stem cell transplantation, with engraftment rates of 86.4%. Post hematopoietic stem cell transplantation event-free survival was 81.8%.[3]

Study NI-0501-05, was a multicenter follow-up study to collect safety and outcome data for patients who received emapalumab through NI-0501-04 and compassionate use programs. Patients were followed for 1 year after hematopoietic stem cell transplantation or after the last infusion of emapalumab for patients in whom hematopoietic stem cell transplantation was not performed. The most commonly reported adverse events in the NI-0501-04/05 studies during the pre-conditioning phase included bacterial, fungal and viral infections (56%) and aggravated condition aggravated (50.0%), which includes HLH reactivation, flare, worsening. Other commonly reported AEs during the pre-conditioning period included hypertension (41.2%), infusion-related reactions (27%), and pyrexia (24%). In addition, 56% of patients in the NI-0501-04/-05 studies reported infections during the preconditioning period. During the post-conditioning period, the most commonly reported adverse events were pyrexia (52.2%) and hypertension (43.5%), along with common hematopoietic stem cell transplantation complications. As

of July 20, 2017, 20 of 51 patients receiving drug through compassionate use programs and the NI-0501-04/05 studies had fatal adverse events. The fatal adverse events were reported to be consistent with complications of HLH, rather than being related to treatment with emapalumab. Regarding serious adverse events, the most common ones reported during the pre-conditioning period were aggravated HLH (18.9%) and respiratory failure (9.4%). Common serious adverse events after hematopoietic stem cell transplantation included condition aggravated and engraft failure (11.1% each), and pyrexia, acute GVHD in intestine, engraftment syndrome, *Klebsiella* sepsis, and septic shock (7.4% each). Adverse events resulting in treatment withdrawal included disseminated histoplasmosis and HLH worsening. Additionally, in the NI-0501-04/05 studies, necrotizing fasciitis and disseminated histoplasmosis have been reported to be related to emapalumab.[3,4]

Henter et al completed HLH-2004 as a follow up to HLH-94, the first prospective international treatment study for hemophagocytic lymphohistiocytosis (HLH), where diagnosis was based on five criteria which included fever, splenomegaly, bicytopenia, hypertriglyceridemia and/or hypofibrinogenemia, and hemophagocytosis. In HLH-2004 three additional criteria were added and include low/absent NK-cell-activity, hyperferritinemia, and high-soluble interleukin-2-receptor levels. For diagnosis, five of these eight criteria must be fulfilled, unless a family history or genetic test is consistent with HLH. HLH-2004 chemo-immunotherapy includes initial treatment with etoposide, dexamethasone, & cyclosporine and intrathecal therapy with methotrexate and corticosteroids in select patients. Subsequent hematopoietic stem cell transplantation is recommended for patients with familial disease or molecular diagnosis, and patients with severe and persistent, or reactivated, disease.[2]

U.S. Food and Drug Administration (FDA)

This section is to be used for informational purposes only. FDA approval alone is not a basis for coverage.

Gamifant is indicated for the treatment of adult and pediatric (newborn and older) patients with primary HLH with refractory, recurrent or progressive disease or intolerance with conventional HLH therapy.[1]

References

1. Gamifant [package insert]. Waltham, MA: Sobi; May 2022.
2. Henter JI, Horne A, Aricó M, et al. HLH-2004: Diagnostic and therapeutic guidelines for hemophagocytic lymphohistiocytosis. Pediatr Blood Cancer. 2007;48:124-31.
3. Study NI-0501-04. Data on file, Sobi Pharmaceuticals.
4. Study NI-0501-05. Data on file, Sobi Pharmaceuticals.

Policy History/Revision Information

Date	Summary of Changes
12/01/2023	• Routine review; no content changes • Archived previous policy version CSLA2022D0077F

Instructions for Use

This Medical Benefit Drug Policy provides assistance in interpreting UnitedHealthcare standard benefit plans. When deciding coverage, the federal, state or contractual requirements for benefit plan coverage must be referenced as the terms of the federal, state or contractual requirements for benefit plan coverage may differ from the standard benefit plan. In the event of a conflict, the federal, state or contractual requirements for benefit plan coverage govern. Before using this policy, please check the federal, state or contractual requirements for benefit plan coverage. UnitedHealthcare reserves the right to modify its Policies and Guidelines as necessary. This Medical Benefit Drug Policy is provided for informational purposes. It does not constitute medical advice.

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independent professional medical judgment of a qualified health care provider and do not constitute the practice of medicine or medical advice.