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Section:	Prescription Drugs	**Effective Date:**	July 1, 2022
Subsection:	Endocrine and Metabolic Drugs	**Original Policy Date:**	December 7, 2018
Subject:	Gamifant	**Page:**	1 of 6

Last Review Date: June 16, 2022

Gamifant

Description

Gamifant (emapalumab-lzsg)

Background

Hemophagocytic lymphohistiocytic (HLH) most frequently affects infants from birth to 18 months of age but can also affect children and adults of all ages. It is an aggressive and life-threatening syndrome characterized by excessive inflammation and tissue destruction due to abnormal immune activation. Unregulated activation of immune cells (macrophages, NK cells, CTLs) result in hypersecretion of interferon gamma (IFNγ). Gamifant (emapalumab-lzsg) is a monoclonal antibody that binds to and neutralizes interferon gamma (IFNγ), which plays a pivotal role in the pathogenesis of HLH by being hypersecreted (1-2).

Regulatory Status

FDA-approved indication: Gamifant is an interferon gamma (IFNγ) blocking antibody indicated for the treatment of: (2)

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

Testing should be done for latent tuberculosis infections using the purified protein derivative (PPD) or IFNγ release assay and patients should be evaluated for tuberculosis risk factors prior to initiating Gamifant. Tuberculosis prophylaxis should be administered to patients at risk for tuberculosis, or known to have a positive PPD test result, or positive IFNγ release assay (2).

Patients should be monitored for tuberculosis, adenovirus, Epstein-Barr virus (EBV), and cytomegalovirus (CMV) every 2 weeks and as clinically indicated (2).

Prophylaxis should be administered for Herpes Zoster, *Pneumocystis jirovecii*, and for fungal infections prior to Gamifant administration. For patients who are not receiving baseline dexamethasone treatment, dexamethasone should be started at a daily dose of at least 5 to 10 mg/m^2 the day before Gamifant treatment begins. For patients who were receiving baseline dexamethasone, they may continue their regular dose provided the dose is at least 5 mg/m^2. Dexamethasone can be tapered according to the judgment of the treating physician (2).

Gamifant may increase the risk of fatal and serious infections to include specific pathogens favored by IFNγ neutralization, including mycobacterium, Herpes Zoster virus, and *Histoplasma capsulatum*. Patients receiving Gamifant should be closely monitored for signs and symptoms or infection and a complete diagnostic workup and appropriate antimicrobial therapy should be initiated. Patients should not be given live or live attenuated vaccines during therapy and for at least 4 weeks after the last dose of Gamifant (2).

Safety and effectiveness of Gamifant have been established in pediatric patients, newborn and older, with primary HLH that is reactivated or refractory to conventional therapies (2).

Related policies

Policy

This policy statement applies to clinical review performed for pre-service (Prior Approval, Precertification, Advanced Benefit Determination, etc.) and/or post-service claims.

Gamifant may be considered **medically necessary** in patients with primary hemophagocytic lymphohistiosis (HLH) and if the conditions indicated below are met.

Gamifant may be considered **investigational** for all other indications.

Prior-Approval Requirements

Diagnosis

Patients must have the following:

1. Primary hemophagocytic lymphohistiocytosis (HLH)

a. The diagnosis has been confirmed by genetic testing or using clinical findings, including lab tests and symptoms (see Appendix 1)

AND ALL of the following:

1. Will be given concurrently with dexamethasone
2. Patient has had an inadequate response, intolerance, or contraindication to at least **ONE** of the following:
    a. Etoposide
    b. Cyclosporine A
    c. Anti-thymocyte globulin
3. Prescriber agrees to monitor for tuberculosis, adenovirus, EBV, and CMV
4. Absence of active infection
5. **NOT** given concurrently with live or live attenuated vaccines

Prior – Approval *Renewal* Requirements

Diagnosis

Patients must have the following:

1. Primary hemophagocytic lymphohistiocytosis (HLH)

AND ALL of the following:

1. Will be given concurrently with dexamethasone
2. Hematopoietic stem cell transplantation (HSCT) has **NOT** been performed
3. **NO** unacceptable toxicity
4. Prescriber agrees to monitor for tuberculosis, adenovirus, EBV, and CMV
5. Absence of active infection
6. **NOT** given concurrently with live or live attenuated vaccines

Policy Guidelines

Pre - PA Allowance

None

Prior - Approval Limits

Duration 12 months

Prior – Approval *Renewal* Limits

Same as above

Rationale

Summary

Gamifant (Emapalumab-lzsg) is a monoclonal antibody that binds to and neutralizes interferon gamma (IFNγ), which is thought to play a major role in pathogenesis of hemophagocytic lymphohistiocytosis. Safety and effectiveness of Gamifant have been established in pediatric patients, newborn and older, with primary HLH that is reactivated or refractory to conventional therapies (2).

Prior authorization is required to ensure the safe, clinically appropriate and cost-effective use of Gamifant while maintaining optimal therapeutic outcomes.

References

1. McCain, K. Eckstein, O. Clinical features and diagnosis of hemophagocytic lymphohistiocytosis. UpToDate. April 14, 2022.
2. Gamifant [package insert]. Waltham, MA: Sobi Inc.; June 2020.

Policy History

Date	Action
December 2018	Addition to PA
March 2019	Annual review
June 2019	Annual review. Added requirement for confirmed diagnosis of HLH by genetic testing or using clinical findings and added Appendix 1 diagnostic criteria per SME
December 2020	Annual review and reference update
June 2021	Annual review and reference update
June 2022	Annual review and reference update

Keywords

This policy was approved by the FEP® Pharmacy and Medical Policy Committee on June 16, 2022 and is effective on July 1, 2022.

Appendix 1 - List of Diagnostic Criteria for HLH

1. Fever (≥38.5°C)
2. Splenomegaly
3. Peripheral blood cytopenias defined as at least two of the following:
    a. Hemoglobin < 9 g/dL (infants less than 4 weeks of age < 10 g/dL)
    b. Platelets < 100 x 10^9/L
    c. Neutrophils < 1.0 x 10^9/L
4. Hypertriglyceridemia or hypofibrinogenemia defined by one of the following:
    a. Fasting triglycerides ≥2.0 mmol/L or > 3 SD of the normal value for age
    b. Fibrinogen ≤1.5 g/L
5. Hemophagocytosis in bone marrow, spleen, or lymph nodes
6. Low or absent natural killer cell activity
7. Ferritin ≥500 mcg/L
8. Soluble CD25 (soluble IL2Rα) ≥2400 U/mL)