Prior Authorization Review Panel

CHC-MCO Policy Submission

A separate copy of this form must accompany each policy submitted for review.
Policies submitted without this form will not be considered for review.

Plan: PA Health & Wellness	**Submission Date: 02/01/2021**
Policy Number: PA.CP.PHAR.402	**Effective Date: 01/01/2018** **Revision Date: 01/2021**
Policy Name: Emapalumab-lzsg (Gamifant)	

Type of Submission – Check all that apply:

- ☐ **New Policy**
- ✓ **Revised Policy***
- ☐ **Annual Review - No Revisions**
- ☐ **Statewide PDL** - *Select this box when submitting policies for Statewide PDL implementation and when submitting policies for drug classes included on the Statewide PDL.*

***All revisions to the policy must be highlighted using track changes throughout the document.**

Please provide any changes or clarifying information for the policy below:

1Q 2021 annual review: added criteria for diagnosis confirmation per clinical trial inclusion criteria; references reviewed and updated.

Name of Authorized Individual (Please type or print): **Auren Weinberg, MD**	**Signature of Authorized Individual:** 

Clinical Policy: Emapalumab-lzsg (Gamifant)

Reference Number: PA.CP.PHAR.402
Effective Date: 01.2019
Last Review Date: 01.2021

Coding Implications
Revision Log

Description
Emapalumab-lzsg (Gamifant™) is an interferon gamma (IFNγ) blocking antibody.

FDA Approved Indication(s)
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.

Policy/Criteria
Provider must submit documentation (such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria.

It is the policy of health plans affiliated with PA Health & Wellness® that Gamifant is **medically necessary** when the following criteria are met:

I. Initial Approval Criteria

A. Primary Hemophagocytic Lymphohistiocytosis (must meet all)**:**

1. Diagnosis of primary HLH (i.e., familial (inherited) HLH);
2. Prescribed by or in consultation with a hematologist;
3. Failure of conventional HLH therapy that includes an etoposide- and dexamethasone-based regimen, unless contraindicated or clinically significant adverse effects are experienced;
4. Documentation of a scheduled bone marrow or hematopoietic stem cell transplantation (HSCT) or identification of a transplant donor is in process;
5. Dose does not exceed 10 mg/kg per dose, two doses per week.

Approval duration: 2 months

B. Other diagnoses/indications

1. Refer to the off-label use policy for the relevant line of business if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): PA.CP.PMN.53.

II. Continued Therapy

A. Primary Hemophagocytic Lymphohistiocytosis (must meet all)**:**

1. Currently receiving medication via PA Health & Wellness benefit or member has previously met initial approval criteria or the Continuity of Care policy (PA.LTSS.PHAR.01) applies;
2. Member is responding positively to therapy – including but not limited to improvement in any of the following parameters:
   a. Fever reduction;
   b. Splenomegaly;

c. Central nervous system symptoms;
d. Complete blood count;
e. Fibrinogen and/or D-dimer;
f. Ferritin;
g. Soluble CD25 (also referred to as soluble interleukin-2 receptor) levels;

3. If request is for a dose increase, new dose does not exceed 10 mg/kg per dose, two doses per week.

Approval duration: 6 months

B. Other diagnoses/indications (must meet 1 or 2)**:**

1. Currently receiving medication via PA Health & Wellness benefit and documentation supports positive response to therapy or the Continuity of Care policy (PA.LTSS.PHAR.01) applies.
   Approval duration: Duration of request or 6 months (whichever is less); or
2. Refer to the off-label use policy for the relevant line of business if diagnosis is NOT specifically listed under section III (Diagnoses/Indications for which coverage is NOT authorized): PA.CP.PMN.53.

III. Diagnoses/Indications for which coverage is NOT authorized:

A. Non-FDA approved indications, which are not addressed in this policy, unless there is sufficient documentation of efficacy and safety according to the off label use policy – PA.CP.PMN.53 or evidence of coverage documents.

IV. Appendices/General Information

Appendix A: Abbreviation/Acronym Key
FDA: Food and Drug Administration
HLH: hemophagocytic lymphohistiocytosis
HSCT: hematopoietic stem cell transplantation

Appendix B: Therapeutic Alternatives
This table provides a listing of preferred alternative therapy recommended in the approval criteria. The drugs listed here may not be a formulary agent for all relevant lines of business and may require prior authorization.

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
etoposide (Toposar®)	150 mg/m^2 IV twice weekly for 2 weeks and then weekly for an additional 6 weeks. Continuation therapy from week 9 until HSCT: 150 mg/m^2 every alternating second week	150 mg/m^2 per dose
dexamethasone	10 mg/m^2 PO or IV for 2 weeks followed by 5 mg/m^2 for 2 weeks, 2.5 mg/m^2 for 2 weeks, 1.25 mg/m^2 for 1 week, and 1 week of tapering	See dosing regimen

Drug Name	Dosing Regimen	Dose Limit/ Maximum Dose
	Continuation therapy from week 9 until HSCT: 1010 mg/m^2 for 3 days every second week	

Therapeutic alternatives are listed as Brand name® (generic) when the drug is available by brand name only and generic (Brand name®) when the drug is available by both brand and generic.

Appendix C: Contraindications/Boxed Warnings
None reported

Appendix D: General Information

- Overall response in the Gamifant clinical trial (NCT01818492**)** was evaluated using an algorithm that included the following objective clinical and laboratory parameters: fever, splenomegaly, central nervous system symptoms, complete blood count, fibrinogen and/or D-dimer, ferritin, and soluble CD25 (also referred to as soluble interleukin-2 receptor) levels.
  - Complete response was defined as normalization of all HLH abnormalities (i.e., no fever, no splenomegaly, neutrophils > 1x10^9/L, platelets > 100x10^9/L, ferritin < 2,000 µg/L, fibrinogen > 1.50 g/L, D-dimer < 500 ug/L, normal CNS symptoms, no worsening of sCD25 > 2-fold baseline).
  - Partial response was defined as normalization of ≥ 3 HLH abnormalities.
  - HLH improvement was defined as ≥ 3 HLH abnormalities improved by at least 50% from baseline.
- Gamifant is currently not indicated for the treatment of secondary HLH. Secondary HLH generally presents in adults and is triggered by autoimmune disease, infections, or cancer. Treatment for secondary HLH is focused on the triggering condition.

V. Dosage and Administration

Indication	Dosing Regimen	Maximum Dose
Primary HLH	1 mg/kg IV twice per week (every three to four days)	10 mg/kg/dose

VI. Product Availability

Single-dose vial: 10 mg/2 mL, 50 mg/10 mL

VII. References

1. Gamifant Prescribing Information. Geneva, Switzerland: Novimmune; November 2018. Available at: https://www.accessdata.fda.gov/drugsatfda_docs/label/2018/761107s000lbl.pdf. Accessed November 17, 2020.
2. Henter JI, Samuelsson-Horne AC, Arico M, et al. Treatment of hemophagocytic lymphohistiocytosis with HLH-94 immunochemotherapy and bone marrow transplantation. Blood 2002; 100 (7): 2367-72.
3. Chesshyre E, Ramanan AV, Roderick MR. Hemophagocytic Lymphohistiocytosis and Infections: An update. The Pediatric Infectious Disease Journal March 2019; 38(3): e54-e56.

4. Bergsten E, Horne AC, Arico 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): 2728-38.
5. Locatelli F, Jordan MB, Allen C, et al. Emapalumab in Children with Primary Hemophagocytic Lymphohistiocytosis. N Engl J Med. 2020 May 7;382(19):1811-1822. doi: 10.1056/NEJMoa1911326. PMID: 32374962.

Coding Implications
Codes referenced in this clinical policy are for informational purposes only. Inclusion or exclusion of any codes does not guarantee coverage. Providers should reference the most up-to-date sources of professional coding guidance prior to the submission of claims for reimbursement of covered services.

HCPCS Codes	Description
C9050	Injection, emapalumab-lzsg, 1 mg
J9210	Injection, emapalumab-lzsg, 1 mg

Reviews, Revisions, and Approvals	Date	P&T Approval Date
Policy created	01.19	
1Q 2020 annual review: no significant changes; references reviewed and updated.	01/2020	
1Q 2021 annual review: added criteria for diagnosis confirmation per clinical trial inclusion criteria; references reviewed and updated.	01/2021	