RXADVANCE
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Clinical Policy Title:	Emapalumab-lzsg (Gamifant)
Policy Number:	RxA.142
Drug(s) Applied:	Emapalumab-lzsg (Gamifant™)
Original Policy Date:	01/2020
Last Review Date:	04/21/2020
Line of Business Policy Applies to:	Commercial

Background

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

Dosing Information

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

Dosage Forms

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

Clinical Policy

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

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 or oncologist or immunologist or transplant specialist;
3. Failure of conventional primary HLH therapy including etoposide, dexamethasone, cyclosporin A 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.
6. Member does not have any active infections caused by to specific pathogens favored by IFNγ neutralization, including mycobacteria, Herpes Zoster virus, and Histoplasma Capsulatum
7. Documentation of latent tuberculosis (TB) test result (purified protein derivative test or IFNγ release assay) showing negative result or supporting documentation showing member is taking prophylactic TB treatment (eg: isoniazid) if member is at risk for TB, or known to have a positive test result.
8. Members should have documented concurrent dexamethasone therapy or plan to initiate it

Approval duration: 2 months OR up to date of HSCT or BMT, whichever is sooner

II. Continued Therapy Approval

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

1. Currently receiving medication that has been authorized by RxAdvance or member has previously met initial approval criteria listed in this policy;
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: Up to 6 months OR up to date of HSCT or BMT, whichever is sooner

III. Appendices

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®)	Initial therapy for first 8 weeks: 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 or BMT: 150 mg/m^2 every alternating second week in combination with daily oral cyclopsorin	150 mg/m^2 per dose
dexamethasone	Initial therapy: 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	See dosing regimen

	1 week of tapering Continuation therapy from week 9 until HSCT or BMT: 10 mg/m^2 for 3 days every second week	
Cyclosporin A	Continuation therapy: Starting at week 9, 6mg/kg daily in divided doses (target trough level 200 mcg/L)	N/A

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.

References

1. Gamifant Prescribing Information. Geneva, Switzerland: Novimmune; November 2018. Available at: https://www.accessdata.fda.gov/drugsatfda_docs/label/2018/761107s000lbl.pdf. Accessed April 21, 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. Chesshyr E, Ramanan AV, Roderick MR. Hemophagocytic Lymphohistiocytosis and Infections: An update. The Pediatric Infectious Disease Journal Publish Ahead of Print. DOI: 10.1097/INF.0000000000002248.

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.

Review/Revision History	Review/Revised Date	P&T Approval Date
Policy was established	01/2020	02/07/2020

Added tuberculosis testing criteria to initial approval	04/2020	