Policy Title:	emapalumab-lzsg
Policy Number:	RxA.142
Drug(s) Applied:	Gamifant®
Original Policy Date:	02/07/2020
Last Review Date:	10/19/2023
Line of Business Policy Applies to:	All lines of business (except Medicare)

Criteria

I. Initial Approval Criteria

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

1. Diagnosis of primary HLH [i.e., familial (inherited) HLH]
2. Diagnosis is confirmed based on one of the following (a, b, or c):
   a. Genetic mutation known to cause HLH;
   b. Family history consistent with primary HLH;
   c. Five out of the following 8 criteria needing to be fulfilled:
      i. Fever (temperature > 38.5 C for > 7 days);
      ii. Splenomegaly;
      iii. Cytopenias affecting 2 of 3 lineages in the peripheral blood: hemoglobin < 9, platelets < 100 x 10^9 /L, neutrophils < 1 x 10^9 /L);
      iv. Hypertriglyceridemia (fasting triglycerides >3 mmol/L or ≥ 265 mg/dL) and/or hypofibrinogenemia (≤ 1.5 g/L);
      v. Hemophagocytosis in bone marrow, spleen, or lymph nodes with no evidence of malignancy;
      vi. Low or absent NK-cell activity;
      vii. Ferritin ≥ 500 mcg/L or soluble CD25 > 2400 U/mL);
      viii. Soluble CD25 ≥ 2400 U/mL;
3. Prescribed by or in consultation with a hematologist, oncologist, immunologist, or transplant specialist;
4. Trial and failure of conventional primary HLH therapy including etoposide, dexamethasone, cyclosporine A ± intrathecal methotrexate unless contraindicated or clinically significant adverse effects are experienced;
5. Documentation of a scheduled bone marrow or hematopoietic stem cell transplantation (HSCT) or identification of a transplant donor is in process;
6. Dose does not exceed 10 mg/kg per dose, two doses per week;

Approval Duration
Commercial: 2 months
Medicaid: 2 months

II. Continued Therapy Approval

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

1. Member is currently receiving medication that has been authorized by RxAdvance or the member has 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
Commercial: 6 months
Medicaid: 6 months

References

1. Pessoa FS, Gonçalves VC, Lacerda EM da CB. Haemophagocytic lymphohistiocytosis secondary to intrauterine cytomegalovirus infection. Rev Inst Med trop S Paulo. 2021;63:e15. Available at: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7924979/. Accessed October 18, 2022.
2. 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. Available at: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5785801/. Accessed October 18, 2022.
3. Jordan MB, Allen CE, Weitzman S, Filipovich AH, McClain KL. How I treat hemophagocytic lymphohistiocytosis. Blood. 2011;118(15):4041-4052. Available at: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3204727/ . Accessed October 18, 2022.
4. La Rosée P, Horne A, Hines M, et al. Recommendations for the management of hemophagocytic lymphohistiocytosis in adults. Blood. 2019 Jun 6;133(23):2465-2477. doi: 10.1182/blood.2018894618. Epub 2019 Apr 16. PMID: 30992265. Available at: https://pubmed.ncbi.nlm.nih.gov/30992265/. Accessed October 18, 2022

Review/Revision History	Review/Revision Date	P&T Approval Date
Policy was established	01/2020	02/07/2020
Policy was reviewed: 1. Added tuberculosis testing criteria to initial approval criteria. 2. References updated.	04/2020	05/21/2020
Policy was reviewed. 1. Policy title table was updated. 2. Initial approval criteria I.A.3 was updated to include intrathecal methotrexate in therapy. 3. Approval duration section was updated for initial and continued therapy approval. 4. Continued therapy criteria II.A.1 was rephrased to "Currently receiving medication that has been authorized by RxAdvance...". 5. Reference reviewed and updated.	01/25/2021	03/09/2021
Policy was reviewed: 1. Initial approval therapy criteria I.A.1 was updated to add a,b,c,d,e,f and g .	11/26/2021	01/17/2022

2. Continued Therapy Approval Criteria II.A.1 was rephrased to "Member is currently receiving medication that has been authorized by RxAdvance...". 3. Reference reviewed and updated.		
Policy was reviewed: 1. Initial Approval Criteria, I.A.2, I.A.2.a, I.A.2.b & I.A.2.c.viii: Updated to include new criteria pertaining to indication Primary Hemophagocytic Lymphohistiocytosis, Diagnosis confirmation. 2. Initial Approval Criteria, I.A.2.c.iii: Updated diagnostic criteria from Cytopenias affecting 2 of 3 lineages in the peripheral blood: hemoglobin < 9, platelets to Cytopenias affecting 2 of 3 lineages in the peripheral blood: hemoglobin < 9, platelets < 100 x 109 /L, neutrophils < 1 x 109 /L). 3. Initial Approval Criteria I.A.6: Updated to remove member does not have any active infections caused by to specific pathogens favoured by IFNγ neutralization, including mycobacteria, Herpes Zoster virus, and Histoplasma Capsulatum; 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 (e.g. isoniazid) if member is at risk for TB, or known to have a positive test result. 4. Initial Approval Criteria I.A.7: Updated to remove members should have documented concurrent dexamethasone therapy or plan to initiate it. 5. Reference reviewed and updated.	10/14/2022	01/17/2023
Policy was reviewed.	10/19/2023	10/19/2023