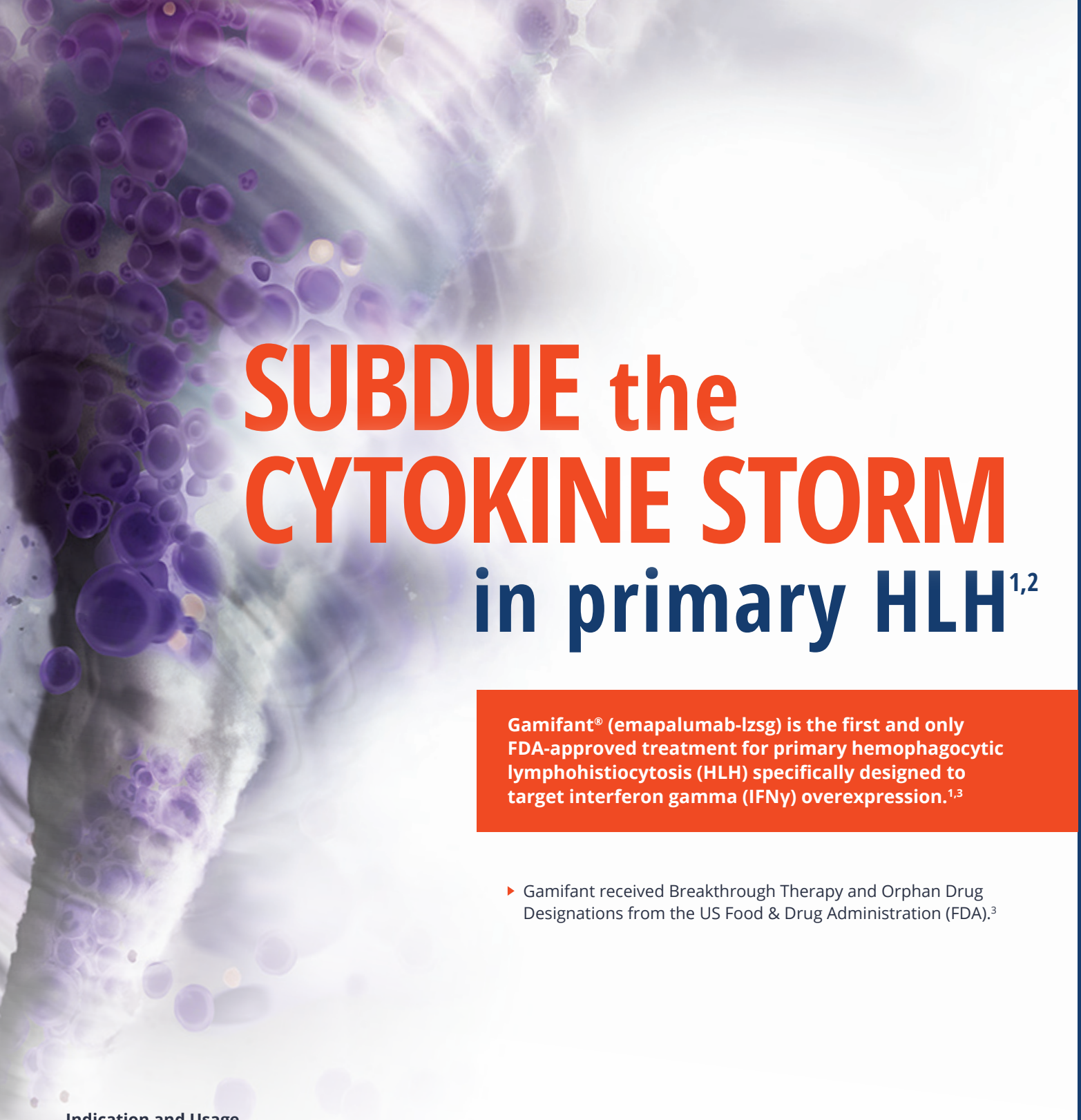

SUBDUE the CYTOKINE STORM in primary HLH[1,2]

Gamifant® (emapalumab-lzsg) is the first and only FDA-approved treatment for primary hemophagocytic lymphohistiocytosis (HLH) specifically designed to target interferon gamma (IFNγ) overexpression.[1,3]

- Gamifant received Breakthrough Therapy and Orphan Drug Designations from the US Food & Drug Administration (FDA).[3]

Indication and Usage

Gamifant® (emapalumab-lzsg) is an interferon gamma (IFNγ)–blocking antibody 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.

Important Safety Information

Before initiating Gamifant, patients should be evaluated for infection, including latent tuberculosis (TB). Prophylaxis for TB should be administered to patients who are at risk for TB or known to have a positive purified protein derivative (PPD) test result or positive IFNγ release assay.

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There's no time to wait[4]

Primary HLH is a rare but fatal health condition that presents as early as infancy and as late as adulthood as a heterogeneous syndrome of rapidly progressive, life-threatening symptoms.[4,5]

Without timely diagnosis and treatment, the median survival is about 2 months.[4] Data show that even with conventional treatments, 50% of patients fail to reach hematopoietic stem cell transplant (HSCT) due to inadequate response.[6]

- **Primary HLH can be challenging to diagnose** due to its variable presentation characterized by fevers, hepatosplenomegaly, severe cytopenias, hyperferritinemia, coagulation defects, liver function impairment, and infections[4,7,8]
- **The goal of treatment in primary HLH patients is to quickly bring hyperinflammation under control.** Where appropriate, a secondary goal of treatment is to prepare patients for HSCT[4,9,10]
- **A central cause of hyperinflammation is the massive overexpression of IFNγ and the resulting "cytokine storm"**—an uncontrolled release of inflammatory cytokines and overactivation of phagocytes that can result in irreversible organ damage and death[5,11]

If you suspect that your patient has primary HLH and have ruled out malignancy, do not wait for confirmed genetic testing to initiate treatment. Closely follow your patient's response to therapy, and for those with refractory, recurrent, or progressive disease or intolerance to conventional therapy **consider Gamifant® (emapalumab-lzsg).**[4,10]

Gamifant is the first and only HLH treatment to target IFNγ, a CENTRAL and UPSTREAM cytokine in the pathogenesis of primary HLH[1,3]

- Gamifant is a monoclonal antibody that **binds to and neutralizes IFNγ**[1]
- This therapy is the **first advance in a quarter century** for patients presenting with the life-threatening, inflammatory symptoms of primary HLH[4,12]

Important Safety Information

During Gamifant treatment, patients should be monitored for TB, adenovirus, Epstein-Barr virus (EBV), and cytomegalovirus (CMV) every 2 weeks and as clinically indicated.

Patients should be administered prophylaxis for herpes zoster, *Pneumocystis jirovecii*, and fungal infections prior to Gamifant administration.

Do not administer live or live attenuated vaccines to patients receiving Gamifant and for at least 4 weeks after the last dose of Gamifant. The safety of immunization with live vaccines during or following Gamifant therapy has not been studied.

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The Gamifant® (emapalumab-lzsg) pivotal trial represents an important milestone in the treatment of primary HLH[1]

PIVOTAL TRIAL DETAILS			
Type	Multicenter, open-label, single-arm study[1]		
No. of patients	34 (7/34 were treatment naïve)[13]		
Median no. of prior agents	3[1]		
Median duration of Gamifant treatment	59 days (range 4-245 days)[1]		
BASELINE DEMOGRAPHICS (n = 27)			
Median age	1 year (range 0.2-13 years)[1]		
Female	52.9%[13]		
Male	47.1%[13]		
DISEASE ACTIVITY / RESPONSE TO CONVENTIONAL TREATMENTS[a,13]			
HLH reactivation: • **After at least partial response** • **After incomplete response and intolerance to previous HLH therapy**	15 (55.6%) 13 (48.1%) 2 (7.4%)		
HLH worsening: • **After partial response** • **After incomplete response** • **After incomplete response and intolerance to previous HLH therapy**	5 (18.5%) 1 (3.7%) 2 (7.4%) 2 (7.4%)		
No response ever achieved	5 (18.5%)		
Intolerance to previous HLH therapy after incomplete response	2 (7.4%)		
PREVIOUS HLH REGIMEN[b,13]			
HLH-94 (dexamethasone, etoposide)[c]	10 (37%)	**Dexamethasone + MPN + CsA**	2 (7.4%)
HLH-2004 (dexamethasone, etoposide, CsA)[d]	9 (33.3%)	**Dexamethasone + CsA**	1 (3.7%)
HLH-HIT (dexamethasone, ATG and etoposide)[e]	4 (14.8%)	**Dexamethasone > 10 mg/m²/day**	1 (3.7%)

ATG, anti-thymocyte globulin; CsA, cyclosporine A; MPN, methylprednisolone.

[a]Patients who entered study with multiple reasons are presented in each reason
[b]Assigned based on the reported drugs the patient received
[c]1 patient also received MPN and anakinra; 1 patient also received alemtuzumab
[d]1 patient also received MPN and ATG
[e]1 patient also received CsA

- **Safety** was evaluated in 34 patients, 7 of whom were treatment naïve[1]
- **Efficacy** was evaluated in 27 pediatric patients who had already received conventional HLH therapy. Eighty-two percent of these patients had a genetically confirmed primary HLH diagnosis[1]

Infusion-Related Reactions

Infusion-related reactions, including drug eruption, pyrexia, rash, erythema, and hyperhidrosis, were reported with Gamifant treatment in 27% of patients. In one-third of these patients, the infusion-related reaction occurred during the first infusion.

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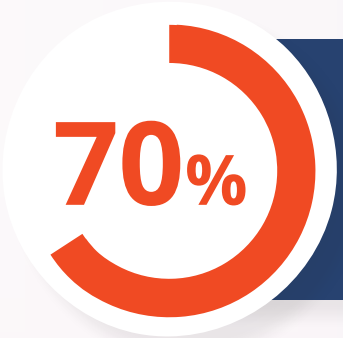
Proven efficacy of a targeted therapy

Gamifant® (emapalumab-lzsg) was shown to be effective treatment for primary HLH in patients with refractory, recurrent, or progressive disease or who were intolerant of conventional treatment.[1]

63% overall response rate (ORR) with Gamifant[1]

(95% CI: 0.42, 0.81; *P* = 0.013)[1]

- **Primary endpoint was overall response rate (ORR)** at the end of treatment, defined as achievement of either complete or partial response or HLH improvement[1]
- **ORR 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[1]
- **Median duration of first response,** defined as time from achievement of first response to loss of first response, was not reached[1]



70% of patients (19/27) proceeded to HSCT[1]

- **Upon completion of the pivotal study**, 22 patients (81%) enrolled in the open-label extension study which monitored patients for up to 1 year after HSCT or after the last Gamifant infusion[1]

Adverse Reactions

In the pivotal trial, the most commonly reported adverse reactions (≥10%) for Gamifant included infection (56%), hypertension (41%), infusion-related reactions (27%), pyrexia (24%), hypokalemia (15%), constipation (15%), rash (12%), abdominal pain (12%), CMV infection (12%), diarrhea (12%), lymphocytosis (12%), cough (12%), irritability (12%), tachycardia (12%), and tachypnea (12%).

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Indication and Usage and Important Safety Information

Indication and Usage

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Additional selected adverse reactions (all grades) that were reported in less than 10% of patients treated with Gamifant included vomiting, acute kidney injury, asthenia, bradycardia, dyspnea, gastrointestinal hemorrhage, epistaxis, and peripheral edema.

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References

1. Gamifant [prescribing information]. Stockholm, Sweden: Swedish Orphan Biovitrum AB; 2020. **2.** Price B, Lines J, Lewis D, Holland N. Haemophagocytic lymphohistiocytosis: a fulminant syndrome associated with multiorgan failure and high mortality that frequently masquerades as sepsis and shock. *S Afr Med J.* 2014;104(6):401-406. **3.** FDA approves first treatment specifically for patients with rare and life-threatening type of immune disease [news release]. Silver Spring, MD: US Food and Drug Administration; November 20, 2018. https://www.fda.gov/newsevents/newsroom/pressannouncements/ucm626263.htm. Accessed July 21, 2020. **4.** Jordan MB, Allen CE, Weitzman S, Filipovich AH, McClain KL. How I treat hemophagocytic lymphohistiocytosis. *Blood.* 2011;118(15):4041-4052. **5.** Sepulveda F, de Saint Basile G. Hemophagocytic syndrome: primary forms and predisposing conditions. *Curr Opin Immunol.* 2017;49:20-26. **6.** Bergsten E, Horne A, Aricó 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):2728-2738. **7.** Marsh RA, Haddad E. How I treat primary haemophagocytic lymphohistiocytosis. *Br J Haematol.* 2018;182(2):185-199. **8.** Kim MM, Yum MS, Choi HW, et al. Central nervous system (CNS) involvement is a critical prognostic factor for hemophagocytic lymphohistiocytosis. *Korean J Hematol.* 2012;47(4):273-280. **9.** George M. Hemophagocytic lymphohistiocytosis: review of etiologies and management. *J Blood Med.* 2014;5:69-86. **10.** Morimoto A, Nakazawa Y, Ishii E. Hemophagocytic lymphohistiocytosis: pathogenesis, diagnosis, and management. *Pediatr Int.* 2016;58(9):817-825. **11.** La Rosée P. Alleviating the storm: ruxolitinib in HLH. *Blood.* 2016;127(13):1626-1627. **12.** Etopophos [prescribing information]. Deerfield, IL: Baxter Healthcare Corporation; 2017. **13.** Data on File. Stockholm, Sweden: Swedish Orphan Biovitrum AB.

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The first step to access is completing the Gamifant Start Form

The Start Form enrolls your patient in Gamifant Patient Services and can be used to initiate a wide range of services and personalized support for you, your staff, your patients, and their caregivers, including:

- Insurance benefit verification
- Coordination of product orders
- Assessment of patient eligibility for financial assistance

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833.597.6530

Gamifant® (emapalumab-lzsg) is supplied as a 10 mg/2 mL (5 mg/mL), 50 mg/10 mL (5 mg/mL), or 100 mg/20 mL (5 mg/mL) solution in single-dose vials. **Gamifant offers flexibility of dosing** and can be incrementally titrated upward or downward according to the clinician's assessment of patient response.[1]

Adverse Reactions

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