



# Gamifant<sup>®</sup> (emapalumab-lzsg) Clinical Overview

## **Indication and Usage**

Gamifant<sup>®</sup> (emapalumab-lzsg) is an interferon gamma (IFN $\gamma$ )-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.

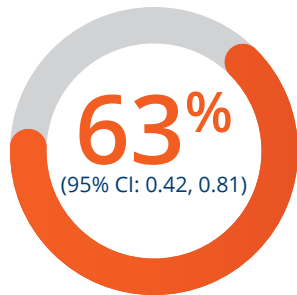
**Please see Important Safety Information on page 6 and accompanying full Prescribing Information.**



## The Only FDA-Approved Drug for Primary HLH

- Gamifant (emapalumab-lzsg) is the only drug approved by the US Food and Drug Administration (FDA) for treating primary hemophagocytic lymphohistiocytosis (HLH) in adult and pediatric patients<sup>1,2</sup>
- Gamifant received Breakthrough Therapy, Rare Pediatric Disease, and Orphan Drug designations from the FDA<sup>3</sup>
- The efficacy of Gamifant was evaluated in a multicenter, open-label, single-arm trial in 27 pediatric patients with suspected or confirmed primary HLH with either refractory, recurrent, or progressive disease during conventional HLH therapy or who were intolerant of conventional HLH therapy<sup>1</sup>

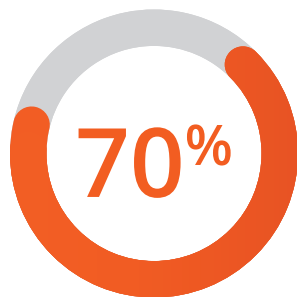
### In patients taking Gamifant



**63%**  
of patients with primary HLH  
achieved an overall response<sup>1,\*</sup>

- All patients were refractory to standard of care (SoC), receiving a median of 3 prior therapies before enrollment in the trial<sup>1</sup>

\*Overall response rate was defined as achievement of either a complete or partial response or HLH improvement.<sup>1</sup>



**70%**  
of patients proceeded to  
hematopoietic stem cell transplant (HSCT)<sup>1</sup>

- Median duration of treatment prior to HSCT was 59 days<sup>1</sup>

### 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 positive purified protein derivative (PPD) test result or positive IFN $\gamma$  release assay.

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

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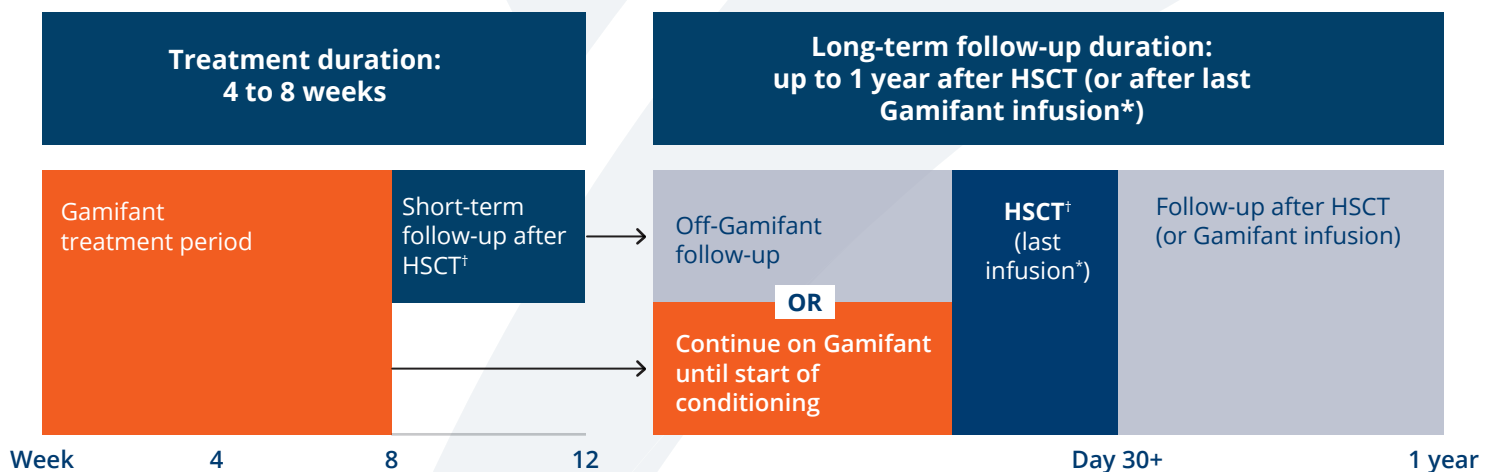
## Pivotal Clinical Trial of Gamifant (emapalumab-lzsg)

### Study design

- A multicenter, open-label, single-arm trial in pediatric patients<sup>1</sup>
- Patients had suspected or confirmed primary HLH with either refractory, recurrent, or progressive disease during conventional HLH therapy or were intolerant of conventional HLH therapy<sup>1</sup>
- Patients received a median of 3 prior therapies before enrollment in the trial<sup>1</sup>
- Twenty-seven patients enrolled and 20 patients (74%) completed the study<sup>1</sup>
- Twenty-two patients enrolled in the open-label extension study for up to 1 year after HSCT or after the last Gamifant infusion<sup>1</sup>

### Pivotal Trial (N=27)<sup>1,4</sup>

### Follow-up Study (N=22)<sup>1,4</sup>



\*Last infusion for patients who do not undergo HSCT.

†HSCT may occur either in the pivotal trial or follow-up study.

### Important Safety Information (continued)

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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## Pivotal Clinical Trial of Gamifant (emapalumab-lzsg) (continued)

### Clinical efficacy

#### Primary Endpoint: Overall Response Rate (ORR)

- The efficacy of Gamifant was based on the ORR at the end of treatment (4 to 8 weeks)<sup>1,4</sup>
- Gamifant induced a clinically and statistically significant ORR in **63%** of patients<sup>1</sup>
  - All patients were refractory to SoC, receiving a median of 3 prior therapies before enrollment in the trial<sup>1</sup>

#### ORR at End of Treatment<sup>1</sup>

		Gamifant (N=27)
ORR	N (%)	<b>17 (63)</b>
	95% CI	<b>0.42, 0.81</b>
	P value*	<b>0.013</b>
Overall Response by Category	Complete response, n (%)	<b>7 (26)</b>
	Partial response, n (%)	<b>8 (30)</b>
	HLH improvement, n (%)	<b>2 (7.4)</b>

\*P value based on exact binomial test at a one-sided significance level of 2.5% comparing proportion of patients with overall response with the null hypothesis of 40%.

#### What is ORR?<sup>1</sup>

ORR is defined as achievement of either a **complete response** or **partial response** or **HLH improvement** evaluated based on objective clinical and laboratory parameters.

##### Complete response

- Normalization of all HLH abnormalities (ie, no fever, no splenomegaly, neutrophils  $>1 \times 10^9/L$ , platelets  $>100 \times 10^9/L$ , ferritin  $<2000 \mu g/L$ , fibrinogen  $>1.50 g/L$ , D-dimer  $<500 \mu g/L$ , normal central nervous system symptoms, and no worsening of soluble CD25 [also referred to as soluble interleukin-2 receptor]  $>2$ -fold baseline)

##### Partial response

- Normalization of  $\geq 3$  HLH abnormalities

##### HLH improvement

- $\geq 3$  HLH abnormalities improved by at least 50% from baseline

#### Key Secondary Endpoint: HSCT

- Treatment with Gamifant enabled **70%** of patients who had already failed previous therapy to proceed to HSCT (median duration of treatment with Gamifant: 59 days)<sup>1</sup>
  - HSCT is the only cure for primary HLH, but it requires that inflammation be controlled prior to transplant<sup>5,6</sup>

### Important Safety Information (continued)

#### 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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## Pivotal Clinical Trial of Gamifant (emapalumab-lzsg) (continued)

### Dosage and administration of Gamifant

Recommended Dosing <sup>1</sup>		
Starting Dose	Frequency	Titration
1 mg/kg intravenously infused over 1 hour	<ul style="list-style-type: none"> <li>Twice per week (every 3 to 4 days)</li> <li>Until HSCT is performed or unacceptable toxicity</li> </ul>	<ul style="list-style-type: none"> <li>May be increased to 3 mg/kg on day 3, then to 6 mg/kg on day 6, and up to a maximum dose of 10 mg/kg on day 9</li> <li>Based on physician's assessment of clinical response</li> </ul>

- After the patient's clinical condition is stabilized, the dose may be decreased to the previous level to maintain clinical response until HSCT<sup>1</sup>
- All patients received concomitant dexamethasone, which was tapered according to the treating physician's judgment<sup>1</sup>

### Gamifant was administered for 4 to 8 weeks—with most patients remaining on the lowest dosages<sup>1</sup>

- The majority of patients remained on the starting dose of 1 mg/kg (44%) or required modest dose escalation to 3 mg/kg to 4 mg/kg (30%)<sup>1</sup>

### Safety information

Most Commonly Reported Adverse Reactions (≥20%) in the Pivotal Trial <sup>1,4,*</sup>	
Adverse Reactions	Gamifant (N=34)
Infections <sup>†</sup>	56%
Hypertension <sup>‡</sup>	41%
Infusion-related reactions <sup>§</sup>	27%
Pyrexia	24%

- In this difficult-to-treat, immunocompromised patient population, refractory to SoC<sup>1</sup>
  - 53% percent experienced serious adverse reactions
  - Only 1 patient discontinued treatment
    - Discontinuation was due to disseminated histoplasmosis

\*Safety was analyzed in treatment-experienced and treatment-naive patients (N=34).

<sup>†</sup>Includes viral, bacterial, and fungal infections, and infections in which no pathogen was identified.

<sup>‡</sup>Includes secondary hypertension.

<sup>§</sup>Includes events of drug eruption, pyrexia, rash, erythema, and hyperhidrosis.

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## Adverse Reactions

In the pivotal trial, the most commonly reported adverse reactions ( $\geq 10\%$ ) 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%).

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, gastro-intestinal hemorrhage, epistaxis, and peripheral edema.

## Please see the full Prescribing Information for Gamifant.

**References:** **1.** Gamifant [prescribing information]. Geneva, Switzerland: Novimmune SA; November 2018. **2.** FDA approves Gamifant® (emapalumab), the first and only treatment for primary haemophagocytic lymphohistiocytosis (HLH) [news release]. Stockholm, Sweden: Sobi; November 20, 2018. <https://www.sobi.com/en/investors/fda-approves-gamifant-emapalumab-first-and-only-treatment-primary-haemophagocytic>. Accessed November 20, 2018. **3.** Novimmune receives Rare Pediatric Disease designation from the FDA for its lead drug emapalumab [news release]. Geneva, Switzerland: Novimmune; September 5, 2017. <https://www.novimmune.com/en/swiss-biopharmaceutical-company/news/2017/novimmune-receives-rare-pediatric-disease-designation-fda-its-lead-drug-emapalumab.html>. Accessed October 25, 2018. **4.** Data on file. Sobi, Inc. Clinical Study Report NI-0501-04. **5.** Henter JL, Horne A, Aricò M, et al; for the Histiocyte Society. HLH-2004: diagnostic and therapeutic guidelines for hemophagocytic lymphohistiocytosis. *Pediatr Blood Cancer*. 2007;48(2):124-131. **6.** Jordan MB, Allen CE, Weitzman S, Filipovich AH, McClain KL. How I treat hemophagocytic lymphohistiocytosis. *Blood*. 2011;118(15):4041-4052.



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