

# INTERFERON GAMMA (IFN $\gamma$ )

A key player in the cytokine storm of primary hemophagocytic lymphohistiocytosis (HLH)<sup>1,2</sup>

## Indication and Usage

Gamifant® (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.

## 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 IFN $\gamma$  release assay.

Please see full Important Safety Information on page 5 and full Prescribing Information [here](#).



**gamifant**<sup>®</sup>  
emapalumab-lzsg

## PRIMARY HEMOPHAGOCYTIC LYMPHOHISTIOCYTOSIS (HLH):

# A condition of life-threatening hyperinflammation<sup>3</sup>

A rare genetic disorder, primary HLH is characterized by a pathological, unregulated cytokine-mediated hyperinflammation that results in life-threatening multiorgan dysfunction.<sup>4</sup> Primary HLH typically occurs in infancy and early childhood, although teen and adult cases have also been identified.<sup>3,5</sup> Without treatment, **median survival of patients is less than 2 months** from a diagnosis of primary HLH, making it critical to initiate therapy quickly so as to manage the hyperinflammatory state caused by this cytokine “storm.”<sup>3</sup>

## A HEALTHY IMMUNE EXPRESSION OF IFN $\gamma$

IFN $\gamma$  is a proinflammatory cytokine that plays a key role in cell communication during a healthy immune response to infections.<sup>2,6-8</sup> It can be produced by a variety of immune cells, including CD4+ T-helper type 1 (TH1) cells, activated CD8+ T cells, natural killer (NK) cells, natural killer T (NKT) cells, and antigen-presenting cells (APCs).<sup>8,9</sup>



### INNATE IMMUNE RESPONSES

IFN $\gamma$  helps eliminate intracellular pathogens by activating macrophages and NK cells.<sup>9</sup>

### ADAPTIVE IMMUNE RESPONSES

IFN $\gamma$  is responsible for both the differentiation and proliferation of T cells.<sup>9</sup>

## IFN $\gamma$ DRIVES HYPERINFLAMMATION TO CREATE THE CYTOKINE STORM<sup>1,2</sup>

While IFN $\gamma$  is not the only cytokine that contributes to primary HLH, it does play a pivotal role in the pathogenesis of the disease.<sup>2</sup> Nonclinical data suggests that elevated IFN $\gamma$  is responsible for the downstream release of other cytokines.<sup>1,5</sup> In primary HLH, the normal IFN $\gamma$  pathway is compromised due to genetic mutations.<sup>4,10</sup>

### 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.

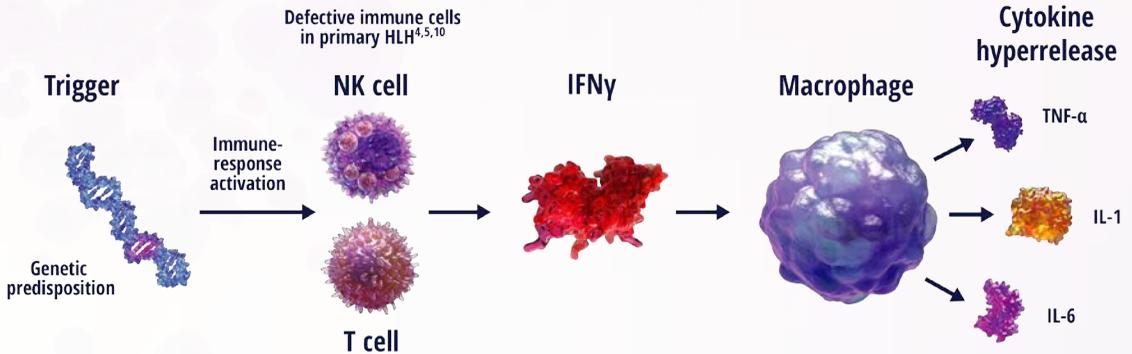
Patients should be administered prophylaxis for herpes zoster, *Pneumocystis jirovecii*, and fungal infections prior to Gamifant administration.

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## UPSTREAM ACTIVATION OF THE CYTOKINE STORM

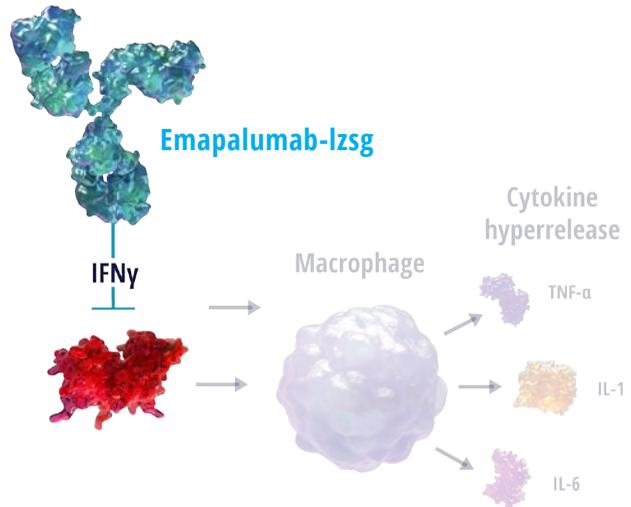
A possible consequence of these genetic mutations is excessive T-cell proliferation and corresponding overexpression of IFN $\gamma$  which drives the activation of macrophages and may result in the phagocytosis of blood cells.<sup>2,5</sup>

At the same time, the release of additional proinflammatory molecules contributes to downstream hypercytokinemia. This cytokine “storm,” in turn, leads to the life-threatening symptoms of primary HLH.<sup>1,2,5</sup>



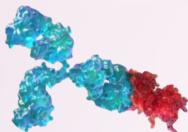
## Gamifant<sup>®</sup> (emapalumab-lzsg) targets IFN $\gamma$ overexpression to subdue the cytokine storm<sup>1,5</sup>

Gamifant is a monoclonal antibody that binds to soluble and receptor-bound forms of IFN $\gamma$  to neutralize its activity, blocking its intracellular signaling to inhibit macrophage activation and the downstream release of proinflammatory cytokines.<sup>1,2,4,5,10,11</sup>



Please see full Important Safety Information on page 5 and full Prescribing Information [here](#).

# Gamifant<sup>®</sup> (emapalumab-lzsg), is the *first and only* FDA-approved treatment specifically developed for primary HLH<sup>1,12</sup>

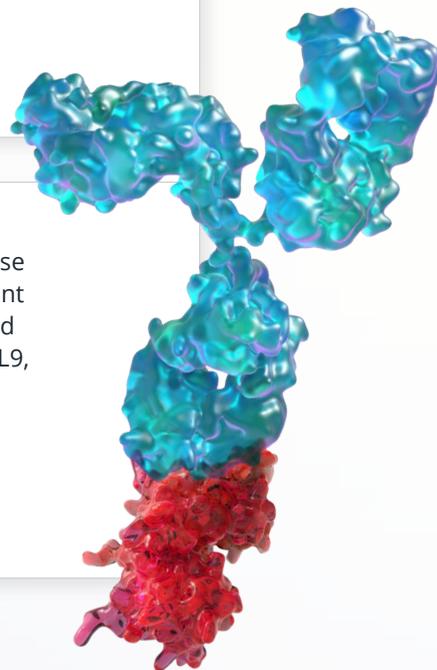


The immediate treatment goal in primary HLH patients is to quickly bring the hyperinflammation under control.<sup>3,10,13</sup> In a departure from conventional, immunosuppressive therapies, Gamifant uniquely targets IFN $\gamma$  to limit overexpression and subdue the hyperinflammatory symptoms of primary HLH.<sup>1,2,5,10-12</sup>

**Watch a video simulation of IFN $\gamma$  suppression with Gamifant.**  
[Gamifant.com/MOA](https://www.gamifant.com/MOA)

The only FDA-approved therapy for patients with refractory, recurrent, or progressive disease or intolerance to conventional therapy, Gamifant has been proven to cause a rapid and sustained reduction in the plasma concentrations of CXCL9, a chemokine induced by IFN $\gamma$ .<sup>1,2,5,10-12</sup>

**Explore clinical trial data to see how Gamifant might fit in to your practice.**  
[Gamifant.com/Trial](https://www.gamifant.com/Trial)



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# Important Safety Information

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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.

## 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.

## 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, gastrointestinal hemorrhage, epistaxis, and peripheral edema.

**Please see the full Prescribing Information for Gamifant [here](#).**

## WE'RE HERE TO ANSWER YOUR QUESTIONS

Find out more about the only FDA-approved therapy for patients with refractory, recurrent, or progressive primary HLH or intolerance to conventional therapy.

### Gamifant Patient Support Services



833.597.6530

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#### References:

1. Gamifant [prescribing information]. Stockholm, Sweden: Swedish Orphan Biovitrum AB; 2018.
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[Gamifant.com](http://Gamifant.com)



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