gamifant®
emapalumab-lzsg

Guide to Gamifant® (emapalumab-lzsg)

Dosing and Administration

Gamifant® (emapalumab-lzsg) Dosing and Administration

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Important Safety Information

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.

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.

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 (≥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.

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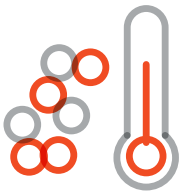
About primary HLH

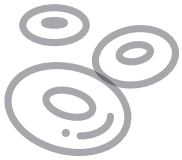
Primary HLH is a genetic disorder that typically occurs in infancy and early childhood, manifesting mostly during the first year of life, but may also occur in teens and adults.[1,2]

Primary HLH presents as a heterogeneous syndrome of rapidly progressive, life-threatening symptoms that can quickly become fatal unless diagnosed and treated. Common symptoms may include[1,3,4]:



- Fever
- Infection
- Rash

- Hepatosplenomegaly
- Liver impairment
- Jaundiced appearance



- Hyperferritinemia
- Coagulation defects
- Severe cytopenia

- Seizure

Massive overexpression of IFNγ is central to the cytokine "storm," the uncontrolled release of inflammatory cytokines and overactivation of phagocytes that give the syndrome its name[5]

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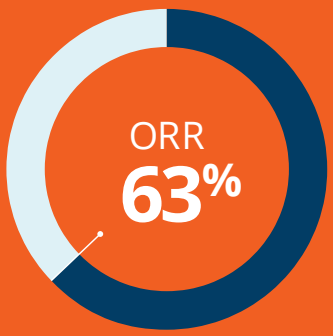
Gamifant® (emapalumab-lzsg) is the first and only approved treatment for primary HLH[6,7]

In clinical studies, Gamifant was shown to be effective treatment for primary HLH in patients with refractory, recurrent, or progressive disease or who were intolerant of conventional treatment.[6]

- Multicenter, open-label, single-arm study of pharmacokinetics, efficacy, and safety of Gamifant in patients with suspected or confirmed primary HLH who had refractory, recurrent, or progressive disease during conventional HLH therapy or were intolerant to it[6]
  - **SAFETY** was evaluated in **34 patients**, 7 of whom were treatment naïve
  - **EFFICACY** was evaluated solely in **27 pediatric patients** who had already received conventional HLH treatment
- Patients had received a median of 3 prior agents as part of standard care before enrollment into the trial; prior regimens included combinations of dexamethasone, etoposide, cyclosporine A, and anti-thymocyte globulin[6]
- Median age of patients in the study was 1 year (range: 0.1-13 years)[6]



Primary endpoint was overall response rate (ORR) at the end of treatment, defined as achievement of either complete or partial response or HLH improvement.[6]

- **In patients with unsatisfactory response to conventional treatments, Gamifant achieved 63% ORR (95% CI: 0.42, 0.81; *P* = 0.013)[6]**

Secondary endpoints included time to response, durability of response, steroid reduction by 50% or more of baseline dose, and patients proceeding to hematopoietic stem cell transplantation (HSCT) when indicated.[7]

- **70% of patients (19/27) proceeded to HSCT[6]**

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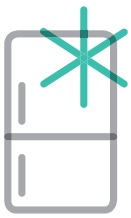
Supplies required for Gamifant® (emapalumab-lzsg) preparation and infusion

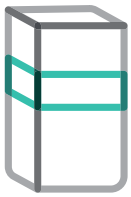
Gamifant is administered as an intravenous infusion over 1 hour twice a week (every 3 to 4 days) until HSCT is performed. You will need the following supplies:

- Gamifant single-dose vials
- Gamma irradiated, latex-free, polyvinyl chloride (PVC)-free syringe (20 mL or 60 mL). Do not use with ethylene oxide-sterilized syringes
- Non-PVC polyolefin infusion bag (dependent on volume needed)
- 0.9% sodium chloride for injection, USP
- Intravenous line with sterile, non-pyrogenic, low-protein binding 0.2 µm in-line filter

Storage and handling



- Store in a refrigerator at 2°C to 8°C (36°F to 46°F). Gamifant contains no preservative.



- Store in original carton to protect from light.

- DO NOT FREEZE OR SHAKE.

- Do not transport via pneumatic tube.

Gamifant Injection is supplied in the following packaging configurations:

- NDC 72171-501-01—containing one 10 mg/2 mL (5 mg/mL) single-dose vial
- NDC 72171-505-01—containing one 50 mg/10 mL (5 mg/mL) single-dose vial

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Premedication and concomitant medications

Premedication

- Administer prophylaxis for herpes zoster, *Pneumocystis jirovecii*, and for fungal infections prior to Gamifant® (emapalumab-lzsg) administration

Concomitant medications

- Gamifant should be given concomitantly with dexamethasone
- For patients who are not receiving baseline dexamethasone treatment, begin dexamethasone at a daily dose of at least 5 to 10 mg/m^2 the day before Gamifant treatment begins
- Patients who are receiving baseline dexamethasone may continue their regular dose provided the dose is at least 5 mg/m^2
- Dexamethasone can be tapered according to the judgment of the treating physician

Infusion-related reactions

- Mild to moderate infusion-related reactions, including drug eruption, pyrexia, rash, erythema, and hyperhidrosis, were reported with Gamifant in 27% of patients
- In one-third of these patients, the infusion-related reactions occurred during the first infusion
- No infusion-related reactions led to premature withdrawal or were reported as serious adverse events

Monitor patients for infusion-related reactions

Interrupt infusion for severe infusion-related reactions and institute appropriate medical management prior to continuing infusion at a slower rate

Important Safety Information

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

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Steps in preparing and administering Gamifant® (emapalumab-lzsg) to patients

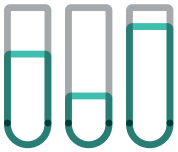
STEP 1 Calculate the Gamifant dose

There are four variables to any Gamifant dose infusion

- Patient weight in kg
- Desired mg/kg dose
- Desired total infusion volume (to be administered over 1 hour)
- Patient condition (restrict total infusion volume; see chart on page 9)

Record actual patient weight

The weight of the patient must be taken prior to preparation of Gamifant for administration, ideally on the same day as the infusion.



Select the patient dose in mg

(Can be 1 mg/kg, 3 mg/kg, 6 mg/kg, or 10 mg/kg) Patient weight (kg) x dose ([selected] mg/kg) = total mg of Gamifant needed

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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STEP 2 Calculate the infusion volume in mL

Recommended infusion volumes based on dose, infusion concentration, and patient weight

Patient Weight (kg)		3	5	10	15	20	25	30	40	50	60	70	90
Dose	Gamifant concentration in infusion solution												
1 mg/kg	0.5 mg/mL	6	10										
1 mg/kg	1 mg/mL			10	15	20	25	30	40	50	60	70	90
3 mg/kg	1 mg/mL	9	15	30	45	60	75	90					
3 mg/kg	2 mg/mL								60	75	90	105	135
6 mg/kg	2 mg/mL	9	15	30	45	60	75	90					
6 mg/kg	2.5 mg/mL								96	120	144	168	216
10 mg/kg	2 mg/mL	15	25	50	75								
10 mg/kg	2.5 mg/mL					80	100	120	160	200	240	280	360

Total mg of Gamifant® (emapalumab-lzsg) needed (from Step 1) ÷ selected mg/mL concentration = Total mL of Gamifant needed

Note: In cases where patient condition requires restriction of total infusion volume, higher concentration of infusion solution than those recommended can be used as long as the final concentration of infusion solution remains ≤ 2.5 mg/mL.

STEP 3 Calculate the number of single-dose vials needed

Total mL needed ÷ 10 = # of 10-mL vials
Add # of 2-mL vials needed to reach desired dose

Depending on the patient's weight and the volume required, using a combination of 10-mL and 2-mL vials may help to avoid waste.

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STEP 4 Select the appropriate bags or syringes

Depending on the dose to be administered and the weight of the patient, the diluted sterile concentrate can be administered either in 20 mL or 60 mL syringes or in a 0.9% sodium chloride for injection, USP infusion bag of the appropriate size, depending on the volume to be infused.

For example, if the volume of the infusion solution (taking into account priming of the infusion line) is ≤ 56 mL, one syringe is to be used:

- 20 mL syringe, when the volume to be delivered is ≤ 16 mL
- 60 mL syringe, when the volume to be delivered is > 16 mL and ≤ 56 mL

Note: Do not use with ethylene oxide-sterilized syringes

If > 56 mL, an infusion bag is to be used:

- 100 mL bag, when the volume to be delivered is ≤ 80mL
- 250 mL bag, when the volume to be delivered is > 80 mL and ≤ 230 mL
- 500 mL bag (if available) or 2 x 250 mL bags, when the volume to be delivered is > 230 mL

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%).

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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STEP 5 Prepare Gamifant® (emapalumab-lzsg) dilution

Prepare the solution for infusion as follows:

- After removing from refrigerator, inspect Gamifant vials visually for particulate matter and discoloration prior to dilution. Gamifant is a clear to slightly opalescent, colorless to slightly yellow liquid. Do not administer if discolored or foreign particulate matter is present
- Withdraw the necessary amount of Gamifant solution and dilute with 0.9% Sodium Chloride Injection, USP to a maximum concentration of 2.5 mg/mL. Do not dilute product to less than 0.25 mg/mL
- Discard any unused portion left in the vial(s). Gamifant vials are for single use only
- The diluted solution can be placed in either a syringe or an infusion bag, depending on the volume needed

- Gently invert the infusion bag or syringe several times to ensure complete and homogeneous distribution of Gamifant

- DO NOT SHAKE
- Once the infusion solution is prepared, it should be clearly labeled for administration to the patient

Please see page 12 for more information on infusion concentration parameters

Storage of diluted solution

Gamifant vials do not contain a preservative. If not administered immediately:

- Store the diluted solution of Gamifant under refrigeration at 2°C to 8°C (36°F to 46°F) for no more than 4 hours from the time of dilution
- If refrigerated, allow the diluted solution to come to room temperature prior to administration
- Do not freeze or shake

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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Parameters to consider for the preparation of the Gamifant® (emapalumab-lzsg) solution for infusion

An appropriate concentration of Gamifant in the infusion solution has to be chosen in order to optimize the final volume of the solution to be infused.

- The maximum volume of non-diluted drug (5 mg/mL) to be administered should not exceed 50% of the total volume of the final solution. Therefore the maximum concentration to be used should be 2.5 mg/mL
- The total volume to be administered should take into account pediatric infusion guidelines:
  - For patients weighing less than 10 kg, the maximum volume to be administered should be 4 mL/kg/hr
  - For patients weighing between 10 and 20 kg, the maximum volume to be administered should be 6 mL/kg/hr

The volume of the infusion solution to be prepared depends on priming or flushing.

- **Priming**

  The volume of the infusion line between the syringe and the intravenous catheter is taken into account in the final volume contained in the syringe or the bag.

- **Flushing**

  The volume in the syringe or bag must be entirely delivered, which means that the infusion line is gently flushed with saline once the infusion is completed. If flushing is part of the infusion process to deliver the full dose, it should be performed immediately after the end of the infusion.

Infusion-Related Reactions

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STEP 6 Administer Gamifant® (emapalumab-lzsg) by IV infusion

Gamifant is administered as an intravenous infusion over 1 hour twice a week (every 3 to 4 days) until HSCT is performed or unacceptable toxicity.

Discontinue Gamifant when a patient no longer requires therapy for the treatment of HLH.

- Administer Gamifant diluted solution intravenously over 1 hour through an intravenous line containing a sterile, non-pyrogenic, low-protein binding 0.2 µm in-line filter
    - The duration of the infusion should be adapted when the volume to be infused is above the usual pediatric infusion recommendations (see table on page 9)
- The infusion should preferably be performed through a central line, although peripheral infusions have been performed with no safety concern
- The volume to be infused will be administered through an infusion pump. To ensure that the exact dose of Gamifant has been given, enter the volume to be administered into the pump, along with the rate at which it is to be infused. Also take into account the infusion process, whether priming or flushing
- Do not infuse Gamifant concomitantly with other agents and do not add any other product to the infusion bag or syringe or infuse simultaneously through the same intravenous line

- Do not store any unused portion of the infusion solution for reuse. Any unused product or waste material should be disposed of in accordance with local requirements

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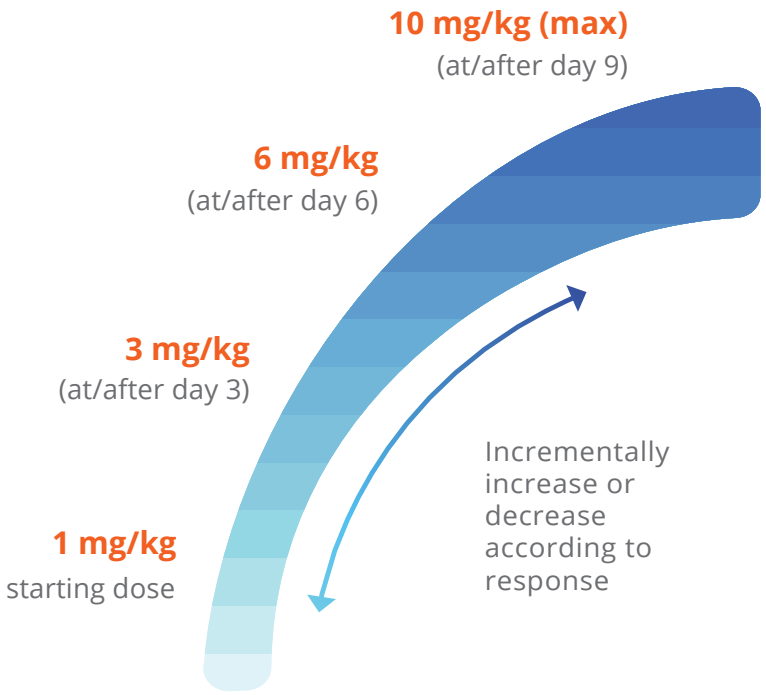
Gamifant® (emapalumab-lzsg) dosing can be modified according to patient response



Gamifant offers flexibility of dosing and can be incrementally titrated upward or downward according to the clinician's assessment of patient response.

After the patient's clinical condition is stabilized, decrease the dose to the previous level to maintain clinical response until HSCT.

Dexamethasone can also be tapered according to the judgment of the treating physician. See page 7 for more details.

Dose increases should be based on both clinician assessment of unsatisfactory improvement in clinical condition, AND at least one of the following:

Platelet count	If baseline < 50,000/mm³ and no improvement to > 50,000/mm³
	If baseline > 50,000/mm³ and less than 30% improvement
	If baseline > 100,000/mm³, any decrease to < 100,000/mm³
Fever	Persistence or recurrence
Neutrophil count	If baseline < 500/mm³ and no improvement to > 500/mm³
	If baseline > 500-1000/mm³ and decrease to < 500/mm³
	If baseline 1000-1500/mm³ and decrease to < 1000/mm³
Ferritin	If baseline ≥ 3000 ng/mL and < 20% decrease
	If baseline < 3000 ng/mL and any increase to > 3000 ng/mL
Splenomegaly	Any worsening
Coagulopathy (both D-dimer and fibrinogen must apply)	D-dimer: if abnormal at baseline and no improvement
	Fibrinogen (mg/dL): if baseline levels ≤ 100 mg/dL and no improvement or if baseline levels > 100 mg/dL and any decrease to < 100 mg/dL

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Start treatment with Gamifant® (emapalumab-lzsg)

Gamifant Patient Services

The first step to access is completing the Start Form

To order Gamifant, you must submit a Start Form. The Start Form can also be used to:

- Initiate insurance benefit verification
- Coordinate product orders through our Specialty Pharmacy or Specialty Distributor
- Assess patient's eligibility for financial assistance

Simply download and complete the Gamifant Start Form found at Gamifant.com and fax it to Gamifant Patient Services at **1-866-895-7204.**

- Be sure to include copies of your patient's insurance and pharmacy benefit cards
- Double-check that the all required fields have been completed so as not to delay access

Once the start form has been received, a member of the Gamifant Patient Services team will contact you to facilitate the ordering process and help ensure that your patient receives their treatment as quickly as possible. **If your order is urgent, please call 1-833-597-6530.**

Urgent order? Questions? We are here to help.

1-833-597-6530

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For more information, please visit:

Gamifant.com

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