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GUIDE TO GAMIFANT

Dosing and Administration for patients with MAS in Still's disease

INDICATION

Gamifant (emapalumab-lzsg) is an interferon gamma (IFNγ)-neutralizing antibody indicated for adult and pediatric (newborn and older) patients with HLH/macrophage activation syndrome (MAS) in known or suspected Still's disease, including systemic Juvenile Idiopathic Arthritis (sJIA), with an inadequate response or intolerance to glucocorticoids, or with recurrent MAS.

IMPORTANT SAFETY INFORMATION

Infections

Gamifant may increase the risk of fatal and serious infections with pathogens including mycobacteria, herpes zoster virus, and histoplasma capsulatum. Do not administer Gamifant in patients with these infections until appropriate treatment has been initiated.

Please see additional Important Safety Information on page 3. Click here for full Prescribing Information for Gamifant.

Gamifant dosing and administration for patients with MAS in Still's disease

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IV=intravenous.

IMPORTANT SAFETY INFORMATION (continued)

Infections (continued)

In patients with HLH/MAS in Still's disease receiving Gamifant in clinical trials, serious infections such as pneumonia, cytomegalovirus infection, cytomegalovirus infection reactivation, and sepsis were observed in 13% of patients.

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Indication and Important Safety Information

INDICATION

Gamifant (emapalumab-lzsg) is an interferon gamma (IFNγ)-neutralizing antibody indicated for adult and pediatric (newborn and older) patients with HLH/macrophage activation syndrome (MAS) in known or suspected Still's disease, including systemic Juvenile Idiopathic Arthritis (sJIA), with an inadequate response or intolerance to glucocorticoids, or with recurrent MAS.

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In patients with HLH/MAS in Still's disease receiving Gamifant in clinical trials, serious infections such as pneumonia, cytomegalovirus infection, cytomegalovirus infection reactivation, and sepsis were observed in 13% of patients.

Evaluate patients for tuberculosis risk factors and test for latent infection prior to initiating Gamifant. Administer tuberculosis prophylaxis to patients at risk for tuberculosis or known to have a positive purified protein derivative (PPD) test result.

Consider prophylaxis for herpes zoster, *Pneumocystis jirovecii*, and fungal infection while receiving Gamifant. Employ surveillance testing during treatment with Gamifant. Closely monitor patients receiving Gamifant for signs or symptoms of infection, promptly initiate a complete diagnostic workup appropriate for an immunocompromised patient, and initiate appropriate antimicrobial therapy.

Increased Risk of Infection With Use of Live Vaccines

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 in patients with HLH/MAS in Still's disease, including pyrexia, headache, paresthesia, bone pain, pruritic rash, and peripheral coldness, were reported with Gamifant treatment in 13% of patients. Infusion-related reactions were reported as mild in 8% of patients and as moderate in 5% of patients.

Monitor patients for infusion-related reactions, which can be severe. Interrupt the infusion for infusion reactions and institute appropriate medical management prior to continuing infusion at a slower rate.

Adverse Reactions

Serious adverse reactions were reported in 12 patients (31%), with the most common serious adverse reaction being pneumonia (5%). Fatal adverse reactions occurred in 2 patients (5%) and included multiple organ dysfunction and circulatory shock.

The most common adverse reactions (≥10%) for Gamifant included viral infection (44%), rash (21%), anemia (18%), leukopenia (15%), thrombosis (15%), bacterial infections (13%), headache (13%), hyperglycemia (13%), infusion-related reactions (13%), abdominal pain (10%), hypertension (10%), pyrexia (10%), and thrombocytopenia (10%).

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About macrophage activation syndrome (MAS)

MAS is a subtype of hemophagocytic lymphohistiocytosis (HLH). HLH can be associated with a variety of underlying conditions, including infection, malignancy, and rheumatic disease. MAS is the term used for HLH that is associated with underlying rheumatic diseases.[1]

MAS is characterized by:

Interferon gamma (IFNγ)-hyperactivated macrophages that release an uncontrolled surge of proinflammatory cytokines[2]

Systemic hyperinflammation that can quickly become life-threatening[3]

IFNγ is a central and upstream mediator of the hyperinflammatory feedback loop in MAS[4]

Signs and symptoms

MAS often presents with a range of nonspecific signs and symptoms, which can make diagnosis a challenge.[5] Some common manifestations of hyperinflammation in patients with MAS include persistent fever, cytopenias, coagulopathies, hyperferritinemia, liver dysfunction, and hepatosplenomegaly.[5-8]

It's imperative to be able to accurately diagnose MAS as quickly as possible and initiate appropriate treatment to avoid life-threatening organ damage.[5,7]

Required supplies for Gamifant administration

Before you begin preparing Gamifant for administration, you will need a few supplies. See below for a list of the available single-dose vial sizes, ancillary supplies, and storage and handling information.

Vial sizes[9]

- **NDC 66658-501-01** containing one **10 mg**/2 mL (5 mg/mL) single-dose vial
- **NDC 66658-505-01** containing one **50 mg**/10 mL (5 mg/mL) single-dose vial
- **NDC 66658-510-01** containing one **100 mg**/20 mL (5 mg/mL) single-dose vial

Supplies needed[9]

- Gamifant single-dose vials
- Gamma-irradiated, or ethylene oxide–sterilized, latex-free, polyvinyl chloride (PVC)-free syringe (20 mL or larger syringe)
- Non-PVC polyolefin infusion bag (dependent on volume needed)
- 0.9% sodium chloride for injection, USP
- Intravenous (IV) line with sterile, non-pyrogenic, low-protein binding, 0.2-µm in-line filter

Storage and handling[9]

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

DO NOT FREEZE OR SHAKE

Store in original carton to protect from light

Do not transport via pneumatic tube

IMPORTANT SAFETY INFORMATION (continued)

Infections (continued)

Evaluate patients for tuberculosis risk factors and test for latent infection prior to initiating Gamifant. Administer tuberculosis prophylaxis to patients at risk for tuberculosis or known to have a positive purified protein derivative (PPD) test result.

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Prophylaxis and live vaccines

Prophylaxis information

- Consider prophylaxis for herpes zoster, *Pneumocystis jirovecii*, and fungal infections prior to Gamifant administration[9]

Increased risk of infection with use of live vaccines

- 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[9]

Monitor patients for infusion-related reactions

Interrupt infusion for infusion-related reactions and institute appropriate medical management prior to continuing infusion at a slower rate[9]

IMPORTANT SAFETY INFORMATION (continued)

Infections (continued)

Consider prophylaxis for herpes zoster, *Pneumocystis jirovecii*, and fungal infection while receiving Gamifant. Employ surveillance testing during treatment with Gamifant.

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Steps in preparing and administering Gamifant to patients

STEP 1: Calculate the Gamifant dose

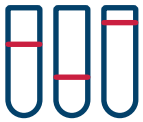
There are 4 variables to any Gamifant dose infusion[9]:

- Patient actual body weight in kg
- Desired mg/kg dose
- Desired total infusion volume in mL (to be administered over 1 hour)
- Patient health condition (restrict total infusion volume; see table on page 8)

Click here to access **Dosing Calculator**

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.[9]



Select the patient dose in mg

Patient weight (kg) x dose ([selected] mg/kg) = total mg of Gamifant needed.

The recommended starting dose for patients with MAS in Still's disease is 6 mg/kg[9]

Infusion-related reactions

- Mild to moderate infusion-related reactions, including pyrexia, headache, paresthesia, bone pain, pruritic rash, and peripheral coldness, were reported with Gamifant in 13% of patients[9]

IMPORTANT SAFETY INFORMATION (continued)

Infections (continued)

Closely monitor patients receiving Gamifant for signs or symptoms of infection, promptly initiate a complete diagnostic workup appropriate for an immunocompromised patient, and initiate appropriate antimicrobial therapy.

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STEP 2: Calculate the total infusion volume and number of vials needed

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												
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 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 concentrations of infusion solution than those recommended can be used as long as the final concentration of infusion solution remains ≤2.5 mg/mL. Do not dilute product to <0.25 mg/mL.[9]

Calculate the number of vials needed per dose of Gamifant

Gamifant is available as 2 mL, 10 mL, or 20 mL vials.[9]

- Total mg of Gamifant needed ÷ 5 mg/mL Gamifant concentration
- Divide by 2 mL, 10 mL, or 20 mL for # of vials of Gamifant
- Vials are for single dose only. Any remaining drug must be discarded

Vial calculation example

If a patient weighs 5 kg and a 6 mg/kg dose is selected, then the total dose of Gamifant needed is 30 mg.

To calculate the number of vials needed for a 30 mg dose, divide by 5 mg/mL.

- 30 mg divided by 5 mg/mL = 6 mL of Gamifant
- 6 mL would require one 10 mL vial of Gamifant, which would produce 4 mL of waste. Or, select three 2 mL vials of Gamifant for exactly 6 mL of drug

IMPORTANT SAFETY INFORMATION (continued)

Increased Risk of Infection With Use of Live Vaccines

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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STEP 3: Select the appropriate bags or syringes[9]

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 larger syringes or in a 0.9% sodium chloride for injection, USP infusion bag of the appropriate size, depending on the volume to be infused.

STEP 4: Prepare Gamifant dilution[9]

- 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 <0.25 mg/mL
- Discard any unused portion left in the vial(s). Gamifant vials are for single dose 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 10 for more information on infusion concentration parameters

Storage of diluted solution[9]

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 (continued)

Infusion-Related Reactions

Infusion-related reactions in patients with HLH/MAS in Still's disease, including pyrexia, headache, paresthesia, bone pain, pruritic rash, and peripheral coldness, were reported with Gamifant treatment in 13% of patients. Infusion-related reactions were reported as mild in 8% of patients and as moderate in 5% of patients.

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STEP 4: Prepare Gamifant dilution (continued)

Parameters to consider for the preparation of Gamifant 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[9]
- 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 IV 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.

Monitor patients for infusion-related reactions
Interrupt infusion for infusion reactions and institute appropriate medical management prior to continuing infusion at a slower rate[9]

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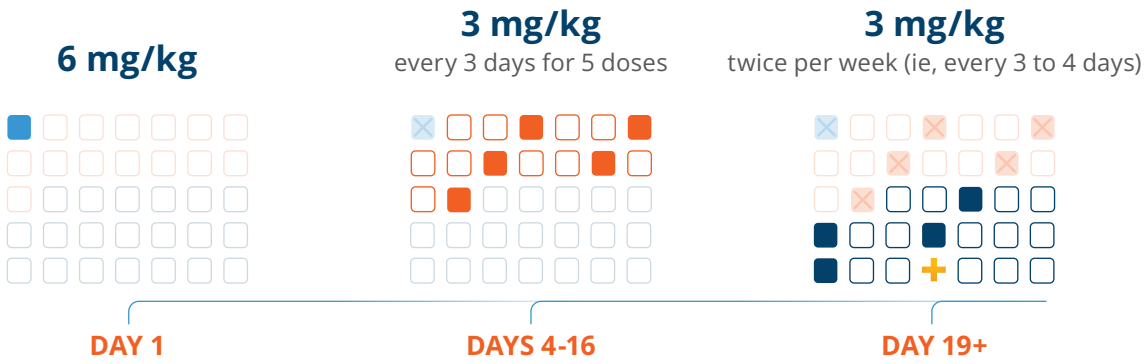
STEP 5: Administer Gamifant by IV infusion

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 larger syringes or in a 0.9% sodium chloride for injection, USP infusion bag of the appropriate size, depending on the volume to be infused.[9]

Gamifant is administered by IV infusion. **The recommended initial dose of Gamifant is 6 mg/kg.** Following this dose, **Gamifant should be administered as follows[9]**:



✚ Continue administering Gamifant twice per week until MAS remission is achieved based on HCP assessment.

- Administer Gamifant diluted solution intravenously over 1 hour through a central or peripheral intravenous line containing a sterile, non-pyrogenic, low-protein binding, 0.2-µm in-line filter[9]
- 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 8)
- 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[9]

Dosing adjustments according to patient response

For patients with unsatisfactory improvement in their clinical condition as assessed by an HCP, Gamifant may be[9]:

Increased to a maximum cumulative dose of **10 mg/kg over 3 days**

AND

1-2 DAYS

Administered **every 2 days or once daily**

- After the patient's clinical condition has improved, consider decreasing the dose to the previous level and assess whether clinical response is maintained[9]
- If the clinical condition is not stabilized while receiving the maximum dosage, consider discontinuing Gamifant[9]

Gamifant is **not contraindicated for concomitant use** with any medication.[9]

IMPORTANT SAFETY INFORMATION (continued)

Adverse Reactions

Serious adverse reactions were reported in 12 patients (31%), with the most common serious adverse reaction being pneumonia (5%). Fatal adverse reactions occurred in 2 patients (5%) and included multiple organ dysfunction and circulatory shock.

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Glucocorticoid tapering

Glucocorticoids can be tapered according to the judgment of the treating physician to help reduce the risk of overexposure.[9,10]

Effect of Gamifant on CYP450 substrates[9]

- The formation of CYP450 enzymes may be suppressed by increased levels of cytokines (such as IFNγ) during chronic inflammation. By neutralizing IFNγ, use of Gamifant may normalize CYP450 activities, which may reduce the efficacy of drugs that are CYP450 substrates due to increased metabolism
- Upon initiation or discontinuation of concomitant Gamifant, monitor for reduced efficacy and adjust dosage of CYP450 substrate drugs as appropriate

IMPORTANT SAFETY INFORMATION (continued)

Adverse Reactions (continued)

The most common adverse reactions (≥10%) for Gamifant included viral infection (44%), rash (21%), anemia (18%), leukopenia (15%), thrombosis (15%), bacterial infections (13%), headache (13%), hyperglycemia (13%), infusion-related reactions (13%), abdominal pain (10%), hypertension (10%), pyrexia (10%), and thrombocytopenia (10%).

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Ordering Gamifant

There are **2 pathways to access Gamifant**. Keep in mind that your institution and the patient's insurance will dictate how Gamifant should be ordered.

McKESSON

Plasma and Biologics Specialty Distributor

Phone: 877-625-2566

Fax 888-752-7626

connect.mckesson.com

Negotiation of supplemental payment with payer: Hospital negotiates payment for costs exceeding the DRG(s)

INPATIENT

Hospital assumes financial responsibility

Patient pays out of pocket to hospital

Infusion center purchases drug and submits claim to payer

OUTPATIENT

Infusion center/physician practice assumes financial responsibility

Patient pays out of pocket to infusion center/ physician practice

DRG=diagnosis-related group.

McKESSON

Biologics

Specialty Pharmacy (SP)

Phone: 800-850-4306, option 2

Fax: 800-823-4506

Biologics dispenses patient-specific drug and delivers directly to pharmacy, infusion center, or other designated location within 24 hours of dispense

INPATIENT **OR** OUTPATIENT

Biologics assumes financial responsibility

Patient pays out of pocket to SP

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gamifant cares™

Support for the journey ahead

Gamifant Cares offers access and reimbursement support to help patients access Gamifant. Gamifant Cares provides information regarding patient insurance coverage and financial assistance information that may be available to help patients with financial needs.

Gamifant Cares can:

- Evaluate a patient's insurance coverage, including benefits investigation, prior authorization, and appeal support
- Provide a Benefit Investigation Summary and, if applicable, any prior authorization requirements
- Identify potential financial assistance options that may be available to help patients with financial needs
- Answer logistical questions and provide information and confirmation around the specialty pharmacy fulfillment process

Field reimbursement and patient support

Sobi's Field Reimbursement Team is an extension of Gamifant Cares. **Your Field Reimbursement Manager (FRM) can educate healthcare professionals and appropriate stakeholders** at institutions about Gamifant Cares and its patient support offerings.

Your FRM can provide information about payer coverage and prior authorization, help to address reimbursement and access issues, and coordinate ongoing support with Gamifant Cares as needed to facilitate patient access to therapy.

The Sobi Field Reimbursement Team can be contacted at **reimbursement@sobi.com**.

For more information, call Gamifant Cares at 1-833-597-6530
Monday-Friday 8:30 AM to 7 PM ET

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Gamifant Cares

Patient assistance and support

Gamifant Cares can provide information about patient assistance programs that may be available to eligible patients.

These offerings include:

- **Gamifant Copay Assistance Program*** is for eligible patients who have commercial prescription insurance. Patients may pay as little as $0 per prescription and may receive up to a maximum benefit of $10,000 per calendar year.
- **Gamifant Patient Assistance Program**† provides Gamifant at no cost to patients who meet the program eligibility requirements.

Transitioning from hospital to outpatient infusion center

While many patients may begin their Gamifant treatment in a hospital setting, they may be discharged once their condition stabilizes. If a patient requires Gamifant treatment in an outpatient setting, Gamifant Cares can assist by evaluating the patient's insurance plan and, when necessary, coordinate with the specialty pharmacy to fill the prescription as the patient transitions to an outpatient setting.

*In order to participate in the Gamifant Copay Assistance Program ("Program"), a patient must have commercial insurance for Gamifant. The Program is not valid for patients whose prescription claims are reimbursed, in whole or in part, by any state or federal government programs, including, but not limited to, Medicaid, Medicare, Medigap, Department of Defense (DoD), Veterans Affairs (VA), TRICARE, Puerto Rico Government Insurance, or any state patient or pharmaceutical assistance program. This offer is not valid for patients paying with cash. The Program is void where prohibited by law. Certain rules and restrictions apply. Sobi reserves the right to revoke, rescind, or amend this offer without notice. **This Program is not insurance.**

†Program subject to eligibility requirements and program terms and conditions. Patients are not eligible for the Program during an inpatient admission.

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For more information about Gamifant dosing and administration, please visit:

GAMIFANT.COM

IMPORTANT SAFETY INFORMATION

Infections

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References: 1. Sen ES, Clarke SLN, Ramanan AV. Macrophage activation syndrome. *Indian J Pediatr.* 2016;83(3):248-253. doi:10.1007/s12098-015-1877-1 **2.** Schulert GS, Grom AA. Macrophage activation syndrome and cytokine directed therapies. *Best Pract Res Clin Rheumatol.* 2014;28(2):277-292. doi:10.1016/j.berh.2014.03.002 **3.** Ravelli A, Minoia F, Davì S, et al; Paediatric Rheumatology International Trials Organisation; Childhood Arthritis and Rheumatology Research Alliance; Pediatric Rheumatology Collaborative Study Group; Histiocyte Society. 2016 classification criteria for macrophage activation syndrome complicating systemic juvenile idiopathic arthritis: a European League Against Rheumatism/American College of Rheumatology/Paediatric Rheumatology International Trials Organisation Collaborative Initiative. *Arthritis Rheumatol.* 2016;68(3):566-576. doi:10.1002/art.39332 **4.** De Benedetti F, Prencipe G, Bracaglia C, Marasco E, Grom AA. Targeting interferon-γ in hyperinflammation: opportunities and challenges. *Nat Rev Rheumatol.* 2021;17(11):678-691. doi:10.1038/s41584-021-00694-z **5.** Lerkvaleekul B, Vilaiyuk S. Macrophage activation syndrome: early diagnosis is key. *Open Access Rheumatol.* 2018;10:117-128. doi:10.2147/OARRR.S151013 **6.** Bseiso O, Zahdeh A, Isayed O, Mahagna S, Bseiso A. The role of immune mechanisms, inflammatory pathways, and macrophage activation syndrome in the pathogenesis of hemophagocytic lymphohistiocytosis. *Cureus.* 2022;14(12):e33175. doi:10.7759/cureus.33175 **7.** Carter SJ, Tattersall RS, Ramanan AV. Macrophage activation syndrome in adults: recent advances in pathophysiology, diagnosis and treatment. *Rheumatology (Oxford).* 2019;58(1):5-17. doi:10.1093/rheumatology/key006 **8.** Crayne C, Cron RQ. Pediatric macrophage activation syndrome, recognizing the tip of the iceberg. *Eur J Rheumatol.* 2019;7(suppl1):S13-S20. doi:10.5152/eurjrheum.2019.19150 **9.** Gamifant (emapalumab-lzsg) prescribing information. Stockholm, Sweden: Sobi, Inc. 2025. **10.** Ericson-Neilsen W, Kaye AD. Steroids: pharmacology, complications, and practice delivery issues. *Ochsner J.* 2014;14(2):203-207.

Please see additional Important Safety Information on page 3. Click here for full Prescribing Information for Gamifant.

For statutory pricing disclosures, click here.

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