GAMIFANT

1. COMPOSITION AND PHARMACEUTICAL FORM

Each ml contains 5 mg of emapalumab. For the full list of excipients, see section 10.

Concentrate for solution for IV infusion

2. INDICATIONS AND USAGE

GAMIFANT is 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.

3. DOSAGE AND ADMINISTRATION

Recommended Dosing

The recommended starting dose of GAMIFANT is 1 mg/kg given as an intravenous infusion over 1 hour twice per week (every three to four days). Doses subsequent to the initial dose may be increased based on clinical and laboratory criteria *[see Dosage and Administration; Dose Modification Based on Response]*.

Administer GAMIFANT until hematopoietic stem cell transplantation (HSCT) is performed or unacceptable toxicity. Discontinue GAMIFANT when a patient no longer requires therapy for the treatment of HLH.

Monitoring to Assess Safety

Before Initiating GAMIFANT Treatment

Conduct testing for latent tuberculosis infections using the purified protein derivative (PPD) or IFNγ release assay and evaluate patients for tuberculosis risk factors prior to initiating GAMIFANT. Administer tuberculosis prophylaxis to patients at risk for tuberculosis, or known to have a positive PPD test result, or positive IFNγ release assay.

During GAMIFANT Treatment

Monitor for tuberculosis, adenovirus, EBV and CMV every 2 weeks and as clinically indicated.

Pre-Medications and Concomitant Medication Information

Pre-Medications

Administer prophylaxis for Herpes Zoster, *Pneumocystis jirovecii*, and for fungal infections prior to GAMIFANT administration.

Concomitant Medications

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. For patients who were receiving baseline dexamethasone, they 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 *[see Clinical Studies (13)]*.

Dose Modification Based on Response

The GAMIFANT dose may be titrated up if disease response is unsatisfactory (see Table 1) *[see Clinical Pharmacology; Pharmacokinetics (11)]*. After the patient's clinical condition is stabilized, decrease the dose to the previous level to maintain clinical response.

Table 1: Dose Titration Criteria

Treatment Day	**GAMIFANT Dose**	**Criteria for Dose Increase**
Day 1	Starting Dose of 1 mg/kg	N/A
On Day 3	Increase to 3 mg/kg	Unsatisfactory improvement in clinical condition, as assessed by a healthcare provider AND at least one of the following: ▪ Fever – persistence or recurrence ▪ Platelet count ▪ If baseline < 50,000/mm^3 and no improvement to > 50,000/mm^3 ▪ If baseline > 50,000/mm^3 and less than 30% improvement ▪ If baseline > 100,000/mm^3 and decrease to < 100,000/mm^3 ▪ Neutrophil count ▪ If baseline < 500/mm^3 and no improvement to > 500/mm^3 ▪ If baseline > 500 -1000/mm^3 and decrease to < 500/mm^3
From Day 6 onwards	Increase to 6 mg/kg	

Treatment Day	GAMIFANT Dose	Criteria for Dose Increase
		▪ If baseline 1000-1500/mm^3 and decrease to < 1000/mm^3 ▪ Ferritin (ng/mL) ▪ 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 ▪ If baseline levels > 100 mg/dL and any decrease to < 100 mg/dL
From Day 9 onwards	Increase to 10 mg/kg	Assessment by a healthcare provider that based on initial signs of response, a further increase in GAMIFANT dose can be of benefit

Instructions for Preparation and Administration

Preparation

GAMIFANT vials are for single-use only.

Prepare the solution for infusion as follows:

- Calculate the dose (mg/kg), total volume (mL) of GAMIFANT required and the number of GAMIFANT vials needed based on patient actual body weight *[see Dosage and Administration; Recommended Dosing (3)]*.
- 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, 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).
- The diluted solution can be placed in either a syringe or an infusion bag, depending on the volume needed.
- Use a gamma irradiated latex-free, polyvinyl chloride (PVC)-free syringe. Do not use with ethylene oxide-sterilized syringes.
- Use a non-PVC polyolefin infusion bag.

Administration

- Administer GAMIFANT diluted solution intravenously over 1 hour through an intravenous line containing a sterile, non-pyrogenic, low-protein binding 0.2 micron in-line filter.
- Do not infuse GAMIFANT concomitantly with other agents and do not add any other product to the infusion bag or syringe.
- 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.

Storage of Diluted Solution

This product does not contain a preservative.

If not administered immediately:

- Store the diluted solution of GAMIFANT under refrigeration at 2°C to 8°C 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. Do not shake.

4. DOSAGE FORMS AND STRENGTHS

GAMIFANT is a clear to slightly opalescent, colorless to slightly yellow preservative-free solution available as:

Concentrate for solution for IV infusion

- 10 mg/2 mL (5 mg/mL) in a single-dose vial
- 50 mg/10 mL (5 mg/mL) in a single-dose vial
- 100 mg/20 mL (5 mg/mL) in a single-dose vial

5. CONTRAINDICATIONS

Hypersensitivity to the active substance or to any of the excipients (listed in section 10).

6. WARNINGS AND PRECAUTIONS

Infections

GAMIFANT may increase the risk of fatal and serious infections to include specific pathogens favored by IFNγ neutralization, including mycobacteria, Herpes Zoster virus, and Histoplasma Capsulatum.

Do not administer GAMIFANT in patients with infections caused by these pathogens until appropriate treatment has been initiated.

In 32% of patients receiving GAMIFANT in clinical trials, serious infections such as sepsis, pneumonia, bacteremia, disseminated histoplasmosis, necrotizing fasciitis, viral infections, and perforated appendicitis were observed. The reported infections were viral (41%), bacterial (35%), fungal (9%), and the pathogen was not identified in 15% of cases.

Evaluate patients for tuberculosis risk factors and test for latent infection (PPD testing, PCR, or IFNγ release assay) 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 *[see Dosage and Administration; Monitoring to assess safety (3)]*.

Administer prophylaxis for Herpes Zoster, *Pneumocystis jirovecii*, and fungal infection to mitigate the risk to patients 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 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.

All infusion related reactions were reported as mild to moderate. Monitor patients for infusion-related reactions. Interrupt infusion for infusion reactions and institute appropriate medical management prior to continuing infusion at a slower rate.

7. EFFECTS ON ABILITY TO DRIVE AND USE MACHINES

There is no information, however emapalumab is not expected to influence or have negligible influence on the ability to drive or use machines.

8. ADVERSE REACTIONS

The following adverse reactions are described elsewhere in the labeling:

- Infections *[see Warnings and Precautions; Infections (6)]*
- Infusion-Related Reactions *[see Warnings and Precautions; Infusion-Related Reactions (6)]*

Clinical Trial Experience

Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a drug cannot be directly compared to rates in the clinical trials of another drug and may not reflect the rates observed in practice.

The safety data described in this section reflect exposure to GAMIFANT in which 34 patients with untreated primary HLH and previously treated patients with primary HLH received GAMIFANT at a starting dose of 1 mg/kg every 3 days with dose increases up to 10 mg/kg *[see Dosage and Administration; Recommended Dosing (3)* and *Clinical Studies (13)]*. The median duration of treatment with GAMIFANT was 59 days (range: 4 to 245 days) and the median cumulative dose was 25 mg/kg (range: 4 to 254 mg/kg).

The median age of study population was 1 year (range: 0.1 to 13 years), 53% were female, and 65% were Caucasian.

Serious adverse reactions were reported in 53% of patients. The most common serious adverse reactions (≥ 3%) included infections, gastrointestinal hemorrhage, and multiple organ dysfunction. Fatal adverse reactions occurred in two (6%) of patients and included septic shock and gastrointestinal hemorrhage.

Disseminated histoplasmosis led to drug discontinuation in one patient. The most commonly reported adverse reactions (≥ 20%) were infections, hypertension, infusion-related reactions, and pyrexia. Adverse reactions reported in ≥ 10% of patients during treatment with GAMIFANT are presented in Table 2.

Table 2: Adverse Reactions Reported in ≥ 10% of Patients with Primary HLH

Adverse Reactions	**GAMIFANT (%) (N = 34)**
Infections[a]	56
Hypertension[b]	41
Infusion-related reactions[c]	27

Adverse Reactions	GAMIFANT (%) (N = 34)
Pyrexia	24
Hypokalemia	15
Constipation	15
Rash	12
Abdominal pain	12
Cytomegalovirus infection	12
Diarrhea	12
Lymphocytosis	12
Cough	12
Irritability	12
Tachycardia	12
Tachypnea	12

[a]Includes viral, bacterial, fungal, and infections in which no pathogen was identified

[b]Includes secondary hypertension

[c]Includes events of drug eruption, pyrexia, rash, erythema, and hyperhidrosis

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.

Immunogenicity

As with all therapeutic proteins, there is potential for immunogenicity. The detection of antibody formation is highly dependent on the sensitivity and specificity of the assay. Additionally, the observed incidence of antibody (including neutralizing antibody) positivity in an assay may be influenced by several factors, including assay methodology, sample handling, timing of sample collection, concomitant medications, and underlying disease. For these reasons, comparison of the incidence of antibodies in the studies described below with the incidence of antibodies in other studies or to other emapalumab products may be misleading.

The immunogenicity of emapalumab has been evaluated using an electrochemiluminescence-based immunoassay (ECLIA). A total of 64 subjects were evaluated for anti-therapeutic antibodies (ATAs) to emapalumab after treatment with GAMIFANT. ATAs were detected in 3/64 subjects (5%) who received GAMIFANT.

Treatment-emergent ATAs were detected in 1/33 (3%) of patients in the primary HLH clinical trial. The ATAs in this patient were found to have neutralizing ability. One patient receiving GAMIFANT through compassionate use developed transient non-neutralizing treatment-emergent ATAs. In both of these patients, ATAs occurred within the first 9 weeks following the initiation of GAMIFANT treatment. In addition, one healthy subject tested positive for ATAs following a single dose of GAMIFANT. No evidence of an altered safety or efficacy profile was identified in the primary HLH patients who developed antibodies to emapalumab.

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorization of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Any suspected adverse events should be reported to the Ministry of Health according to the National Regulation by using an online form: https://sideeffects.health.gov.il

9. DRUG INTERACTIONS

Effect of GAMIFANT on Cytochrome P450 Substrates

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.

10. USE IN SPECIFIC POPULATIONS

Pregnancy

Risk Summary

There are no available data on GAMIFANT use in pregnant women to inform a drug-associated risk of adverse developmental outcomes. In an animal reproduction study, a murine surrogate anti-mouse IFNγ antibody administered to pregnant mice throughout gestation crossed the placental barrier, and no fetal harm was observed *(see Data)*.

The estimated background risk of major birth defects and miscarriage for the indicated population is unknown. All pregnancies have a background risk of birth defect, loss, or other adverse outcomes.

Data

Animal Data

In a mouse embryo-fetal development study, a murine surrogate anti-mouse IFNγ antibody was administered every 3-4 days throughout organogenesis and late gestation at doses of 0, 30, 75 or 150 mg/kg/occasion. The surrogate antibody was detected in the plasma of all treated pregnant

mice and their corresponding fetuses. No maternal toxicity occurred and there was no evidence of teratogenicity or effects on embryo-fetal survival or growth.

Lactation

Risk Summary

There is no information regarding the presence of emapalumab in human milk, the effects on the breastfed child, or the effects on milk production. Published data suggest that only limited amounts of therapeutic antibodies are found in breast milk and they do not enter the neonatal and infant circulations in substantial amounts.

The developmental and health benefits of breastfeeding should be considered along with the mother's clinical need for GAMIFANT and any potential adverse effects on the breastfed child from GAMIFANT or from the underlying maternal condition.

Pediatric Use

Safety and effectiveness of GAMIFANT have been established in pediatric patients, newborn and older, with primary HLH that is reactivated or refractory to conventional therapies. Use of GAMIFANT is supported by a single-arm trial in 27 pediatric patients with reactivated or refractory primary HLH. This study included pediatric patients in the following age groups: 5 patients newborn to 6 months, 10 patients 6 months to 2 years, and 12 patients from 2 years to 13 years *[see Clinical Studies (13)]*.

Geriatric Use

Clinical studies of GAMIFANT did not include sufficient numbers of subjects aged 65 and over to determine whether they respond differently from younger subjects. Other reported clinical experience has not identified differences in responses between the elderly and younger patients.

11. DESCRIPTION

Emapalumab is an interferon gamma (IFNγ) blocking antibody. Emapalumab is produced in Chinese Hamster Ovary cells by recombinant DNA technology. Emapalumab is an IgG1 immunoglobulin with a molecular weight of approximately 148 kDa.

GAMIFANT (emapalumab) concentrate for solution for IV infusion for intravenous use is a sterile, preservative-free, clear to slightly opalescent, colorless to slightly yellow solution provided in single-dose vials that require dilution prior to intravenous infusion.

Each vial contains 10 mg/2 mL, 50 mg/10 mL, or 100 mg/20 mL emapalumab at a concentration of 5 mg/mL. Each mL also contains the following inactive ingredients: sodium chloride, L-histidine monohydrochloride, monohydrate, L-histidine, Super refined Polysorbate 80 (0.005%) and Water for Injection.

12. CLINICAL PHARMACOLOGY

Mechanism of Action

Emapalumab is a monoclonal antibody that binds to and neutralizes interferon gamma (IFNγ). Nonclinical data suggest that IFNγ plays a pivotal role in the pathogenesis of HLH by being hypersecreted.

Pharmacodynamics

IFNγ Inhibition

Emapalumab reduces the plasma concentrations of CXCL9, a chemokine induced by IFNγ.

Cardiac Electrophysiology

At a dose of 3 mg/kg GAMIFANT does not prolong the QT interval to any clinically relevant extent.

Pharmacokinetics

The pharmacokinetics of emapalumab were evaluated in healthy adult subjects and in patients with primary HLH.

Following a 1 mg/kg emapalumab dose, median steady state peak concentration was 44 mcg/mL, which was 2.9 times higher than after the first dose. The median steady state trough concentration was 25 mcg/mL, which was 4.3 times higher than after the first dose. Emapalumab AUC increases slightly more than proportionally between 1 and 3 mg/kg doses, and less than proportionally at 3, 6, and 10 mg/kg doses.

Emapalumab exhibits target-mediated clearance dependent on IFNγ production, which can vary between and within patients as a function of time and can affect the recommended dosage *[see Dosage and Administration; Monitoring to Assess Safety (3)]*. Emapalumab steady state is achieved by the 7th infusion when the IFNγ production is moderate. At high IFNγ production, steady-state is reached earlier due to a shorter half-life.

Distribution

The central and peripheral volumes of distribution in a subject with body weight of 70 kg are 4.2 and 5.6 L, respectively.

Elimination

Emapalumab elimination half-life is approximately 22 days in healthy subjects, and ranged from 2.5 to 18.9 days in HLH patients.

Emapalumab clearance is approximately 0.007 L/h in healthy subjects.

In patients, the total clearance of emapalumab was significantly influenced by the production of IFNγ, demonstrating target mediated clearance of emapalumab.

Metabolism

The metabolic pathway of emapalumab has not been characterized. Like other protein therapeutics, GAMIFANT is expected to be degraded into small peptides and amino acids via catabolic pathways.

Specific Populations

Body weight (2 to 82 kg) was a significant covariate of emapalumab pharmacokinetics, supporting body weight-based dosing.

No clinically significant differences in the pharmacokinetics of emapalumab were observed based on age (0.02 to 56 year), sex (53% Females), race (71.4% Caucasian, 12.2% Asian and 8.2% Black), renal impairment including dialysis, or hepatic impairment (mild, moderate, and severe).

Drug Interaction Studies

No drug-drug interaction studies have been conducted with GAMIFANT.

13. NONCLINICAL TOXICOLOGY

Carcinogenesis, Mutagenesis, Impairment of Fertility

No carcinogenicity or genotoxicity studies have been conducted with emapalumab.

No studies have been conducted to evaluate the effects of emapalumab on fertility; however, no adverse effects on male or female reproductive organs were observed in the 8- or 13-week repeat-dose toxicity studies in cynomolgus monkeys.

14. CLINICAL STUDIES

The efficacy of GAMIFANT was evaluated in a multicenter, open-label, single-arm trial NI-0501-04 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.

Patients were required to fulfill the following criteria for enrollment: primary HLH based on a molecular diagnosis or family history consistent with primary HLH or five out of the 8 criteria fulfilled: fever, splenomegaly, cytopenias affecting 2 of 3 lineages in the peripheral blood (hemoglobin < 9 , platelets < 100 x 10^9/L, neutrophils < 1 x 10^9/L), hypertriglyceridemia (fasting triglycerides > 3 mmol/L or ≥ 265 mg/dL) and/or hypofibrinogenemia (≤ 1.5 g/L), hemophagocytosis in bone marrow, spleen, or lymph nodes with no evidence of malignancy, low or absent NK-cell activity, ferritin ≥ 500 mcg/L, soluble CD25 ≥ 2400 U/mL. Patients had to have evidence of active disease as assessed by treating physician. Patients had to fulfill one of the following criteria as assessed by the treating physician: having not responded or not achieved a satisfactory response or not maintained a satisfactory response to conventional HLH therapy, or intolerance to conventional HLH treatments. Patients with active infections caused by specific pathogens favored by IFNγ neutralization were excluded from the trial (e.g., mycobacteria and *Histoplasma Capsulatum*). Patients received prophylaxis for Herpes Zoster, *Pneumocystis jirovecii*, and fungal infections.

Twenty-seven patients enrolled and received treatment in the study and twenty patients (74%) completed the study. Seven patients (26%) were prematurely withdrawn. Twenty-two patients (81%) enrolled onto the open-label extension study which monitored patients for up to 1 year after HSCT or after the last GAMIFANT infusion (NI-0501-05).

The study treatment duration was up to 8 weeks after which patients could continue treatment on the extension study. All patients received an initial starting dose of GAMIFANT of 1 mg/kg every 3 days. Subsequent doses could be increased to a maximum of 10 mg/kg based on clinical and laboratory parameters interpreted as unsatisfactory response. Forty-four percent of patients remained at a dose of 1 mg/kg, 30% of patients increased to 3-4 mg/kg and 26% of patients increased to 6-10 mg/kg. The median time to dose increase was 27 days (range: 3-31 days) with 22% of patients requiring a dose increase in the first week of treatment.

All patients received dexamethasone as background HLH treatment with doses between 5 to 10 mg/m^2/day. Cyclosporine A was continued if administered prior to screening. Patients receiving methotrexate and glucocorticoids administered intrathecally at baseline could continue these treatments.

In Study NI-0501-04, the median patient age was 1 year (0.2 to 13). Fifty-nine percent of the patients were female, 63% were Caucasian, 11% were Asian, and 11% were Black.

A genetic mutation known to cause HLH was present in 82% of patients. The most frequent causative mutations were FHL3-UNC13D (MUNC 13-4) (26%), FHL2-PRF1 (19%), and Griscelli Syndrome type 2 (19%).

The HLH mutations in the population enrolled are described in Table 3.

Table 3: HLH Mutations in Patients with Primary HLH with Prior Therapy

	GAMIFANT (N=27)
HLH Genetic Confirmation	22 (82)
FHL3 – UNC13D	7 (26)
FHL2 – PRF1	5 (19)
Griscelli Syndrome type 2 (RAB27A)	5 (19)
FHL5 – STXBP2 (UNC18B)	2 (7.4)
FHL4 – STX11	1 (3.7)
X-linked Lymphoproliferative Disorder 1	1 (3.7)
X-linked Lymphoproliferative Disorder 2	1 (3.7)

All patients received previous HLH treatments. Patients received a median of 3 prior agents before enrollment into the trial. Prior regimens included combinations of the following agents: dexamethasone, etoposide, cyclosporine A, and anti-thymocyte globulin.

At baseline entry into the study, 78% of patients had elevated ferritin levels, thrombocytopenia (70% with platelet count of $< 100 \times 10^9$cells/L), hypertriglyceridemia (67%) with triglyceride level > 3 mmol/L. Central nervous system findings were present in 37% of patients. Forty-one percent of patients had active infections not due to specific pathogens favored by IFNγ neutralization at the time of GAMIFANT initiation.

The efficacy of GAMIFANT was based upon overall response rate (ORR) at the end of treatment, defined as achievement of either a complete or partial response or HLH improvement. 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. Complete response was defined as normalization of all HLH abnormalities (i.e., no fever, no splenomegaly, neutrophils > $1x10^9$/L, platelets > $100x10^9$/L, ferritin < 2,000 μg/L, fibrinogen > 1.50 g/L, D-dimer < 500 μg/L, normal CNS symptoms, no worsening of sCD25 > 2-fold baseline). Partial response was defined as normalization of ≥ 3 HLH abnormalities. HLH improvement was defined as ≥ 3 HLH abnormalities improved by at least 50% from baseline.

Table 4: Overall Response Rate at End of Treatment

	GAMIFANT (N=27)
Overall Response Rate	
N (%)	17 (63)
(95% CI)	(0.42, 0.81)
p-value†	0.013
Overall Response by Category	
Complete response, n (%)	7 (26)
Partial response	8 (30)
HLH improvement	2 (7.4)

†p-value based on Exact Binomial Test at a one-sided significance level of 2.5% comparing proportion of patients with overall response to hypothesized null hypothesis of 40%.
CI = confidence interval

The median duration of first response, defined as time from achievement of first response to loss of first response, is not reached (range: 4-56+ days). Seventy percent (19/27) of patients proceeded to HSCT.

15. HOW SUPPLIED/STORAGE AND HANDLING

GAMIFANT (emapalumab) concentrate for solution for I.V infusion is a sterile, clear to slightly opalescent, colorless to slightly yellow solution supplied in the following packaging configuration:

containing one 10 mg/2 mL (5 mg/mL) single-dose vial

containing one 50 mg/10 mL (5 mg/mL) single-dose vial

containing one 100 mg/20 mL (5 mg/mL) single-dose vial

Store GAMIFANT in a refrigerator at 2ºC to 8ºC in original carton to protect from light. Do not freeze or shake. This product contains no preservative.

The expiry date of the product is indicated on the packaging materials.

Not all pack sizes may be marketed.

16. REGISTRATION HOLDER

Truemed Ltd.,

10 Beni Gaon St., Poleg Industrial Park,

P.O.B 8105, Netanya 4250499

17. MANUFACTURER

Swedish Orphan Biovitrum AB (publ)
Stockholm, Sweden

18. REGISTRATION NUMBER

174-81-37435

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