PATIENT PACKAGE INSERT IN ACCORDANCE WITH THE PHARMACISTS' REGULATIONS (PREPARATIONS) – 1986

The medicine is dispensed with a doctor's prescription only

Gamifant

Concentrated solution for preparation of a solution for intravenous infusion

Active ingredient:

Each 1 ml of Gamifant contains emapalumab 5 mg

For inactive and allergenic ingredients in the medicine, see section 2 under "Important information about some of the ingredients of the medicine" and section 6 "Further information".

Read the leaflet carefully in its entirety before using the medicine. This leaflet contains concise information about the medicine. If you have further questions, refer to the doctor or pharmacist.

This medicine has been prescribed to treat your ailment. Do not pass it on to others. It may harm them even if it seems to you that their ailment is similar.

1. WHAT IS THE MEDICINE INTENDED FOR?

Gamifant is intended for the treatment of adult and pediatric (from birth and onward) patients with primary hemophagocytic lymphohistiocytosis (HLH) with refractory, recurrent or progressive disease or intolerance to conventional HLH therapy.

Therapeutic group: Selective immunosuppressants.

HLH is a rare and life-threatening acute inflammatory syndrome caused by proliferation and hyperactivation of the immune system.

The syndrome is caused by a genetic defect and primarily occurs in children, with most cases occurring in the first year of the patient's life.

The symptoms of HLH are generally ascribed to the hyperactivity of the immune system, e.g., enlargement of the spleen and liver.

If the disease is left untreated, HLH may lead to life-threatening multiple organ failure and to an increased risk of death as a result of a serious inflammation.

2. BEFORE USING THE MEDICINE

Do not use the medicine if:

- You are sensitive (allergic) to the active ingredient emapalumab or to any of the additional ingredients contained in the medicine (see section 6 "Further information").

Special warnings regarding use of the medicine

Before and during treatment with Gamifant, tell the doctor if:

- You were recently vaccinated or you are due to receive any vaccine. Do not undergo vaccination with a live or attenuated vaccine during treatment with Gamifant and for at least 4 weeks from the end of treatment with the medicine.
- you have an **infection**. This medicine affects the immune system and may lower the ability of your immune system to fight infections, including herpes zoster (shingles) infections, histoplasmosis (a fungal infection that can affect the lungs) and mycobacterial infection such as tuberculosis.
- you had tuberculosis in the past or you or a family member was recently in close contact with someone sick with tuberculosis. The doctor will check you and may perform a tuberculosis test before you receive Gamifant. If you are at risk, the doctor may give you medicines to treat tuberculosis.

In addition, you will be given prophylactic treatment for shingles, fungal infections and a certain type of lung inflammation to reduce the risk of their onset during the course of treatment with Gamifant.

During the course of treatment or shortly after, you may experience infusion-related reactions. These may include skin reactions, fever, excessive sweating, rash and redness.

Tests and follow-up

During the course of treatment with Gamifant, the doctor will monitor you every two weeks and as clinically recommended for tuberculosis, adenovirus, Epstein-Barr virus (EBV) and cytomegalovirus (CMV).

Drug interactions

If you are taking, or have recently taken, other medicines, including non-prescription medicines and nutritional supplements, tell the doctor or pharmacist.

Pregnancy and breastfeeding

Pregnancy

There is no information regarding the effect of Gamifant on the unborn baby.

If you are pregnant, think you are pregnant or are planning to become pregnant, talk to the doctor before you start treatment with the medicine.

Breastfeeding

It is not known if Gamifant passes into breast milk. If you are breastfeeding or plan to breastfeed, talk to your doctor before using this medicine. You and your doctor will decide if you should stop breastfeeding or stop/abstain from treatment with Gamifant, considering the benefit of breastfeeding to the child and the benefit of treatment to the woman.

Driving and operating machinery

There is no information, but Gamifant is not expected to affect or has a negligible effect on the ability to drive or operate machinery.

Important information about some of the ingredients of the medicine

Gamifant contains sodium.

Each vial of 10 mg contains 5.75 mg sodium, equivalent to 0.29% of the maximum daily intake recommended by the World Health Organization, which is 2 grams of sodium per adult.

Each vial of 50 mg contains 28.75 mg sodium, equivalent to 1.44% of the maximal daily consumption recommended by the World Health Organization, which is 2 grams of sodium per adult.

Each vial of 100 mg contains 57.5 mg sodium, equivalent to 2.87% of the maximal daily consumption recommended by the World Health Organization, which is 2 grams of sodium per adult.

3. HOW SHOULD THE MEDICINE BE USED?

Always use the medicine according to the doctor's instructions. Check with the doctor or pharmacist if you are uncertain regarding the dosage and treatment regimen of the preparation.

The dosage and treatment regimen will be determined by the doctor only.

The usual dosage is generally:

The dose of the medicine will be calculated by the doctor based on your body weight. The usual starting dose is 1 mg per kg body weight and is given twice a week.

The doctor will closely assess your reaction to the medicine and may change the dosage given and decide to increase the dosage or to give the dose more or less frequently.

Do not exceed the recommended dose.

Mode of administration

Gamifant will be given to you by a doctor or nurse through a drip into the vein (intravenous infusion). The duration of the infusion is approximately one hour. During the infusion, you will be closely monitored for side effects.

If you accidentally took a higher dosage/ if you forget to take the medicine

Since this medicine is given by a doctor or nurse, it is unlikely that you will receive a higher dosage or miss a dose. If you are concerned, refer to a doctor or nurse.

Adhere to the treatment as recommended by the doctor. Even if there is an improvement in your health, do not stop treatment with the medicine without consulting the doctor.

Do not take medicines in the dark! Check the label and the dose each time you take medicine. Wear glasses if you need them. If you have further questions regarding use of the medicine, consult the doctor or pharmacist.

4. SIDE EFFECTS

As with any medicine, use of Gamifant may cause side effects in some users.

Do not be alarmed when reading the list of side effects. You may not suffer from any of them.

Refer to your or your child's doctor immediately if you notice any of the side effects below.

The most common serious side effects reported include infections, gastrointestinal bleeding and multiorgan failure.

Other reported side effects observed during or after the treatment:

- the most common (≥20%) side effects reported were infections, high blood pressure, infusion-related reactions and fever.
- side effects reported in 10% or more patients were hypokalemia (low potassium in the blood), constipation, rash, abdominal pain, cytomegalovirus (CMV), diarrhea, lymphocytosis (high lymphocytes in the blood), cough, nervousness, increased heart rate and rapid breathing.

Additional side effects reported in less than 10% of the patients on Gamifant included: vomiting, severe kidney damage, weakness, slow heart rate, shortness of breath, gastrointestinal bleeding, nosebleed and peripheral edema.

As with all protein-based treatments, there is a possibility of development of an undesirable immunogenic effect – a reaction that results in generation of antibodies against the medicine, that reduces/cancels the therapeutic effects of the medicine and may cause various complications.

In patients with primary HLH who developed antibodies against emapalumab, no change in the safety or efficacy profile was identified.

If a side effect occurs, if one of the side effects worsens, or if you suffer from a side effect not mentioned in the leaflet, consult the doctor.

Side effects can be reported to the Ministry of Health by clicking on the link "Report Side Effects of Drug Treatment" found on the Ministry of Health homepage (www.health.gov.il) that directs you to the online form for reporting side effects, or by entering the link: https://sideeffects.health.gov.il

5. HOW SHOULD THE MEDICINE BE STORED?

Avoid poisoning! This medicine and any other medicine should be kept in a safe place out of the reach and sight of children and/or infants in order to avoid poisoning. Do not induce vomiting unless explicitly instructed to do so by the doctor.

Do not use the medicine after the expiry date (exp. date) that appears on the package. The expiry date refers to the last day of that month.

Storage conditions:

Before opening – store refrigerated at 2°C-8°C. Do not freeze or shake. Store in the original package to protect from light. The medicine does not contain preservatives.

Diluted medicine – store the diluted Gamifant solution refrigerated at 2°C-8°C for no more than 4 hours after diluting.

Do not use this medicine if you notice that the solution is discolored or if foreign particles are visible.

6. FURTHER INFORMATION

In addition to the active ingredient, the medicine also contains:

sodium chloride; L-histidine monohydrochloride, monohydrate; L-histidine; super refined polysorbate 80 (0.005%) and water for injection.

What the medicine looks like and the contents of the package:

Gamifant is a clear to slightly opaque, colorless to yellowish solution provided in single-use vials and requires dilution before intravenous infusion.

Gamifant packages include one vial containing 2 ml, 10 ml or 20 ml.

Not all package sizes may be marketed.

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Manufacturer and address: Swedish Orphan Biovitrum, Sweden

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Registration number of the medicine in the National Drug Registry of the Ministry of Health:

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