Patient leaflet in accordance with the Pharmacists' Regulations (Medicinal Products) - 1986

This medicine is dispensed with a doctor's prescription only

MARGENZA 25mg/ml

Intravenous injection

Active ingredient: Each 10ml vial contains 250mg margetuximab.

For the list of excipients in the medicinal product, please see section 6: “Additional information”.

Read the entire leaflet carefully before you start using the medicine. This leaflet contains concise information about the medicine. If you have any further questions, contact the physician or the pharmacist.

1. What is the medicine intended for?

MARGENZA is intended, in combination with chemotherapy, for the treatment of adult patients with metastatic HER2-positive breast cancer who have received two or more prior anti-HER2 regimens, at least one of which was for metastatic disease.

Therapeutic group: antineoplastic agents, monoclonal antibodies (mAbs).

2. Before using this medicine:

Do not use the medicine if:

- You are hypersensitive (allergic) to the active ingredient or any of the other ingredients that this medicine contains (see section 6: “Additional information”).

Special warnings regarding the use of this medicine:

Infusion-Related Reactions (IRRs)

MARGENZA can cause infusion-related reactions (IRRs) (see section 4: "side effects").

These effects will be monitored during MARGENZA administration and as clinically indicated after completion of infusion. Medications and emergency equipment will be available for immediate use to treat IRRs. If you experience dyspnea or clinically significant hypotension, MARGENZA infusion will be interrupt and medical therapy will be given. Monitoring will occur until resolution of signs and symptoms.

If you experience mild or moderate IRRs, premedications will be considered, including antihistamines, corticosteroids, and antipyretics, and infusion rate will be decreased.

Left Ventricular Cardiac Dysfunction

Left ventricular cardiac dysfunction can occur with MARGENZA. Withholding of treatment with MARGENZA may be required in some cases of decrease in left ventricular ejection fraction (LVEF) from pretreatment. Permanent discontinuation of MARGENZA may be required if LVEF decline persists for greater than 8 weeks, or if dosing is interrupted on greater than 3 occasions due to LVEF decline.

Tests and follow-up:

Before you start and during treatment period the physician will conduct a thorough cardiac assessment, including history, physical examination and echocardiogram or MUGA scan. Echocardiogram or MUGA scan is recommended to be peformed 4 weeks prior to initiation of MARGENZA and every 3 months during and upon completion of MARGENZA. If MARGENZA is withheld for significant left ventricular cardiac dysfunction, repeat measurement will be performed at 4-week intervals.

Children and adolesence: This medicine is not intended for children and adolesence under 18 years of age. Safety and effectiveness of MARGENZA have not been established in children and adolesence under 18 years of age.

Elderly: No overall differences in efficacy were observed between patients ≥ 65 years of age compared to younger patients. There was a higher incidence of serious adverse reactions observed in patients age 65 years or older compared to younger patients, including adverse reactions associated with potential cardiotoxicity.

Drug interactions:

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

Anthracyclines

Patients who receive anthracyclines less than 4 months after stopping MARGENZA may be at increased risk of cardiac dysfunction. Avoid anthracycline-based therapy for up to 4 months after stopping MARGENZA. If concomitant use is unavoidable, cardiac function should be closely monitored.

Pregnancy, breast-feeding and fertility:

Pregnancy and fertility

There are no available data on the use of MARGENZA in pregnant women to inform the drug-associated risk. Based on findings in animals and mechanism of action, MARGENZA can cause fetal harm when administered to a pregnant woman.

Exposure to MARGENZA during pregnancy or within 4 months prior to conception can result in fetal harm. Females of reproductive potential should use effective contraception during treatment and for 4 months following the last dose of MARGENZA.

Women who receive MARGENZA during pregnancy or within 4 months prior to conception should be monitored for decreased amniotic fluid that surrounds the fetus (oligohydramnios).

Breast-feeding

There is no information regarding presence of MARGENZA in human milk, effects on the breastfed child, or effects on milk production. Published data suggest human IgG is present in human milk but does not enter neonatal or infant circulation in substantial amounts.

Driving and using machines:

Margenza has a minor influence on the ability to drive or use machines. Dizziness and somnolence may occur during treatment with Margenza. If you experiencing infusion-related symptoms you should avoid driving and useing machines until symptoms abate.

Important information regarding some of the ingredients of the medicine:

This medicine contains 50.4 mg sodium (main component of cooking/table salt) per dose (60 kg patient, 15 mg/kg dose). This is equivalent to 2.5% of the recommended maximum daily dietary intake of sodium for an adult.

3. How to use the medicine?

The medicinal product will be administered by healthcare professional only and according to the doctor’s instructions.

Check with your doctor or pharmacist if you are uncertain about the dosage and treatment regimen of the medicinal product.

The dosage and treatment regimen will be determined only by the doctor. The commonly recommended dose is 15 mg/kg, administered as an intravenous infusion over 120 minutes for the initial dose, then over a minimum of 30 minutes, every 3 weeks for all subsequent doses until disease progression or unacceptable toxicity.

On days when both MARGENZA and chemotherapy are to be administered, MARGENZA may be administered immediately after chemotherapy completion.

Do not exceed the recommended dose.

Before starting MARGENZA and during treatment LVEF will be assessed. MARGENZA dosing will be withheld for at least 4 weeks for any of the following:

- ≥16% absolute decrease in LVEF from pretreatment values.
- LVEF below institutional limits of normal (or 50% if no limits are available) and ≥ 10% absolute decrease in LVEF from pretreatment values.

MARGENZA dosing may be resumed if, within 8 weeks, LVEF returns to normal limits and absolute decrease from baseline is ≤ 15%.

MARGENZA will be permanently discontinued if LVEF decline persists for greater than 8 weeks, or if dosing is interrupted on greater than 3 occasions for LVEF decline.

In patients experiencing dyspnea or clinically significant hypotension, infusion will be interrupted. MARGENZA dosing will be permanently discontinued in patients with severe or life-threatening IRRs.

If you did not receive the medicine

If you missed a dose of MARGENZA, the scheduled dose should be administered as soon as possible. The administration schedule will be adjusted to maintain a 3-week interval between doses.

You should continue 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.

If you have any further questions on the use of this medicine, ask your doctor or pharmacist.

4. Side effects

As with any medicine, MARGENZA can cause side effects in some users. Do not be alarmed when reading the list of side effects. You may not experience any of them.

Infusion-Related Reactions

MARGENZA can cause infusion-related reactions (IRRs). Symptoms may include fever, chills, arthralgia, cough, dizziness, fatigue, nausea, vomiting, headache, diaphoresis, tachycardia, hypotension, pruritus, rash, urticaria, and dyspnea.

Please see section 2 under "special warnings regarding the use of this medicine".

Left Ventricular Cardiac Dysfunction

Please see section 2 under "special warnings regarding the use of this medicine".

Embryo-Fetal Toxicity

Please see section 2 under "pregnancy, breast-feeding and fertility".

Very common (appears in more than 1 out of 10 patients) side effects with MARGENZA in combination with chemotherapy

Fatigue/weakness, nausea, diarrhea, vomiting, constipation, headache, fever, hair loss, abdominal pain, peripheral neuropathy (weakness, numbness, pain, and/or tingling in hands and feet), joint and muscle pain, cough, decreased appetite, shortness of breath, infusion-related reactions, redness/swelling and pain on the palms of the hands and soles of the feet (hand-foot syndrome), and pain in arms and legs.

Common (appears in 1-10 out of 100 patients) side effects with MARGENZA in combination with chemotherapy

Dizziness and inflamed/sore mouth, decreased weight, altered perception of taste, rash, trouble falling and/or staying asleep, high blood pressure, and fainting/passing out.

If a side effect appears, if any side effect gets worse or if you suffer from a side effect not mentioned in the leaflet, you should consult the doctor.

Reporting of side effects:

Side effects can be reported to the Ministry of Health by clicking on the link "Report Side Effects of Drug Treatment" that appears on the homepage of the Ministry of Health's website (www.health.gov.il) which links to an online form for reporting side effects, or by the following link: https://sideeffects.health.gov.il/ and by emailing the Registration Holder's Patient Safety Unit at: drugsafety@neopharmgroup.com

5. How to store the medicine?

Store vials refrigerated (2-8°C) in original carton box to protect from light. Do not freeze. Do not shake.

Storage after dilution: The product does not contain preservatives. If diluted infusion solution is not used immediately, it can be stored at room temperature up to 4 hours or stored refrigerated at 2-8°C up to 24 hours. If refrigerated, allow the diluted solution to come to room temperature prior to administration. Do not freeze. Do not shake.

Do not use the medicine after the expiration date (exp. date) appearing on the packaging.

6. Additional information

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

Sucrose, L-arginine hydrochloride, sodium chloride, sodium phosphate monobasic monohydrate, sodium phosphate dibasic heptahydrate, polysorbate 80, water for Injection.

What does the medicine look like and the contents of the package:

MARGENZA is supplied in a 10ml glass vial.

MARGENZA is a clear to slightly opalescent, colorless to pale yellow or pale brown solution. Some visible, translucent, inherent particles may be present.

The package contains 1 or 4 vials. Not all pack sizes may be marketed.

Manufacturer:

MACROGENICS INC.,

Rockville, Maryland, USA.

Registration Holder:

NEOPHARM LTD.,

6 Hashiloach St., P.O.B 7063, Petach-Tikva 4917001.

Registration number of the medicine in the National Drug Registry of the Ministry of Health: 172-18-37089-00

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