PRODUCT INFORMATION

MEPACT 4 mg powder for dispersion concentrate for infusion

Administered via intravenous infusion.

Sterile **Cytotoxic**

ACTIVE INGREDIENT

Each vial contains 4 mg of mifamurtide.

After reconstitution, each 1 mL of suspension in the vial contains 0.08 mg of mifamurtide.

EXCIPIENTS

1-Palmitoyl-2-oleoyl-sn-glycero-3-phosphocholine (POPC) and 1,2-Dioleoyl-sn-glycero-3-phospho-L-serine monosodium salt (OOPS)

PACKAGING INFORMATION

One 50 mL vial with a grey butyl stopper, aluminum seal, and plastic flip-off cap. One sterile MEPACT filter in a blister pack.

Please read these INSTRUCTIONS FOR USE carefully before you start using this medicine, because it contains important information for you.

Keep these instructions for use. You may need to read them again later.

If you have any additional questions, please consult your doctor or pharmacist.

This medicine has been prescribed for you personally, do not give it to others.

During the use of this medicine, if you go to a doctor or hospital, tell your doctor that you are using this medicine.

Follow these instructions exactly. Do not use a dose **higher** or **lower** than the recommended dose for this medicine.

IN THESE INSTRUCTIONS FOR USE:

are included.

What is MEPACT and what is it used for?

MEPACT is a homogeneous (evenly distributed) white or off-white powder. It may be in cake or powder consistency and must be reconstituted into a suspension and then diluted for infusion (intravenous administration).

MEPACT contains the active ingredient mifamurtide, which resembles a component of the cell wall of certain bacteria. It

stimulates your immune system to help your body kill cancer cells.

MEPACT is used to treat osteosarcoma (bone cancer) in children, adolescents, and young adults (aged 2 to 30 years). It is administered in combination with chemotherapy to kill remaining cancer cells to reduce the risk of cancer recurrence after you have undergone surgery to remove the tumor.

Things to consider before using MEPACT

DO NOT USE MEPACT in the following situations

If you are allergic (hypersensitive) to mifamurtide or any of the excipients contained in MEPACT,

If you are using medicines containing cyclosporine or other calcineurin inhibitors,

If you are using high doses of non-steroidal anti-inflammatory drugs (NSAIDs such as acetylsalicylic acid, ibuprofen, and diclofenac, or cyclooxygenase inhibitors such as celecoxib and rofecoxib).

USE MEPACT CAREFULLY in the following situations

If you have or have had blood clots (thrombosis), bleeding (hemorrhage), or inflammation of blood vessels (vasculitis) in your heart or blood vessels, you need to be monitored more closely during MEPACT treatment. If you experience prolonged or worsening symptoms, you should consult your doctor, as MEPACT treatment may need to be postponed or discontinued.

If you have a history of asthma or other respiratory disorders, you should consult your doctor before using MEPACT to see if you can use your asthma medication with MEPACT.

If you have a history of inflammatory or immune system-related diseases or if you have been treated with corticosteroids such as cortisone and dexamethasone, or other drugs that may affect your immune system such as tacrolimus, you should consult your doctor.

If you have an allergic reaction to any medicine, such as rash, shortness of breath, and high blood pressure. If your symptoms worsen, you should consult your doctor, as these effects may be caused by MEPACT.

If you have stomach problems such as nausea, vomiting, and loss of appetite. If your problems increase, you should consult your doctor, as these effects may be caused by MEPACT when used with chemotherapy.

If you experience chills or shivering, or feel warm. You should measure your body temperature because you may have a fever. A low white blood cell count (neutropenia) accompanied by fever can be a sign of a serious infection.

If these warnings apply to you, even at any time in the past, please consult your doctor.

Using MEPACT with food and drink

Since MEPACT is administered intravenously only, no interaction is expected.

Pregnancy

Consult your doctor or pharmacist before using the medicine.

MEPACT should not be used during pregnancy and in women who are not using effective contraception. If you are receiving MEPACT treatment, you should use an effective method of contraception.

MEPACT is not expected to interact with oral contraceptives (birth control pills). *If you realize you are pregnant during your*

treatment, consult your doctor or pharmacist immediately.

Breastfeeding

Consult your doctor or pharmacist before using the medicine.

It is not known whether MEPACT passes into human milk. Your doctor should decide whether you should continue breastfeeding or continue treatment, taking into account the benefits of breastfeeding for your baby and the benefits of MEPACT treatment for you.

Driving and using machines

Some very common and common side effects of MEPACT treatment (dizziness, balance disorder, fatigue, and blurred vision) may affect your ability to drive and use machines.

Do not drive or use machines during your treatment.

Important information about some of the excipients in MEPACT

Sodium: This medicinal product contains less than 1 mmol (23 mg) of sodium per "dose"; i.e., it is essentially "sodium-free".

Use with other medicines

MEPACT should not be used with drugs such as cyclosporine, tacrolimus, which are used to prevent rejection of transplanted organs after transplantation, or with other immunosuppressive drugs, such as cortisone, prednisone, which are used in the treatment of psoriasis.

MEPACT should not be used with non-steroidal anti-inflammatory drugs (NSAIDs) such as acetylsalicylic acid, ibuprofen, or diclofenac, which are used for headache, fever, or pain. MEPACT should not be used with high doses of NSAIDs.

MEPACT should not be used when corticosteroids such as budesonide, prednisone, and dexamethasone, used in the treatment of inflammation, allergy, and asthma, are used regularly.

If used in the same chemotherapy regimen, it is recommended that the timing of doxorubicin or other drugs be different from that of MEPACT.

If you are currently using or have recently used any prescription or non-prescription medicine, please inform your doctor or pharmacist about them.

How to use MEPACT?

Instructions for proper use and dose/frequency of administration:

Your MEPACT treatment will be initiated and conducted under the supervision of a specialist doctor experienced in the treatment of bone cancer. Always use this medicine exactly as your doctor has told you. If you are not sure, ask your doctor.

The recommended dose of MEPACT for all patients is 2 milligrams per square meter of body surface area. It is administered twice a week at intervals of at least three days for the first 12 weeks, followed by once a week for an additional 24 weeks.

Your MEPACT treatment schedule may be adjusted to align with your chemotherapy schedule. If there is a delay in your chemotherapy, your MEPACT schedule does not need to be interrupted; you should complete your 36-week (9-month) MEPACT treatment without interruption.

Route and method of administration:

The lyophilized powder is reconstituted into a liquid suspension, passed through the provided filter, and then diluted again before use. MEPACT is then administered directly into your vein (intravenous) over approximately 1 hour. This procedure is performed by a doctor or nurse who will continuously monitor you during this time. You do not need to be hospitalized to use MEPACT. It can also be used as an outpatient treatment.

For more information on how to administer MEPACT, please refer to the section for healthcare professionals at the end of this leaflet.

Different age groups:

Use in children:
Use in children younger than 2 years is not recommended due to the lack of efficacy and safety data for this age group.

Use in the elderly:
Efficacy and safety data are available for patients up to 30 years of age. Therefore, data are insufficient to recommend the use of MEPACT in patients older than 30 years.

Special use cases:

Kidney/Liver failure:
No dose adjustment is necessary in mild or moderate renal and/or hepatic impairment. Caution should be exercised when using in patients with severe renal or hepatic impairment.

If you have the impression that the effect of MEPACT is too strong or too weak, talk to your doctor or pharmacist.

> **If you have used more MEPACT than you should:**
>
> Since MEPACT will be administered under the supervision of a doctor or nurse, it is unlikely that you will use more MEPACT than necessary. However, if you think you may have used more MEPACT than you should, tell your doctor without delay.
>
> You may experience fever, chills, fatigue, nausea, vomiting, headache, and low or high blood pressure. In such a case of overdose, consult your doctor or the nearest hospital.
>
> *If you have used more MEPACT than you should, talk to your doctor or pharmacist.*

> **If you forget to use MEPACT:**
>
> Since MEPACT will be administered under the supervision of a doctor or nurse, it is unlikely that a dose will be missed. However, if you think a dose of treatment has been missed, tell your doctor without delay.

Effects that may occur when MEPACT treatment is stopped:

You should not stop your MEPACT treatment without talking to your doctor before your treatment period ends; otherwise, your treatment may not be effective.

What are the possible side effects?

Like all medicines, MEPACT may cause side effects in people sensitive to the substances contained in it.

Upon initial use of MEPACT, most patients experience chills, fever, and fatigue. These are typical temporary conditions ranging from mild to moderate and can usually be treated by your doctor, e.g., by administering paracetamol for fever.

Treatment with MEPACT, when used in combination with chemotherapy, can often lead to stomach problems such as nausea, vomiting, and loss of appetite.

If any of the following occurs, stop using MEPACT and IMMEDIATELY inform your doctor or go to the emergency department of the nearest hospital:

If you have a continuous fever or chills lasting more than 8 hours after taking your MEPACT dose, as this may be a sign of infection,

If you experience a skin rash or any respiratory problems (wheezing), or

If you experience stomach discomfort,

These are very serious side effects. If you have any of these, it means you have a serious allergy to MEPACT. You may need urgent medical intervention or hospitalization.

Very common side effects (seen in more than 1 in 10 patients):

fever, chills/shivering, weakness, fatigue, or general discomfort

nausea and/or vomiting, diarrhea or constipation

headache or dizziness

rapid heartbeat

low or high blood pressure (hypertension)

loss of appetite

sweating

pain (including general pain, muscle and/or joint pain, and pain in the back, chest, abdomen, arm, or leg)

cough, difficulty breathing, or rapid breathing

decrease in body temperature

decrease in the number of red blood cells (erythrocytes)

Common side effects (seen in 1 to 10 out of 100 patients):

bluish discoloration of tissues such as skin or gums due to too little oxygen

noticeable increase in the frequency or force of heartbeat

swelling in arms or legs or other swellings

chest discomfort

stomach upset, decreased appetite, or weight loss

redness, swelling, infection, or other local reaction at the injection or catheter site

skin rash or redness, skin inflammation, itching, dry skin, pale or transient reddish appearance

inflammation of the skin, tendons, muscles, or similar body support tissues

inflammation of a vein (phlebitis)

pain in the upper abdomen or chest wall, abdominal distension or pain, indigestion, or liver pain

other pains including neck, shoulder, groin, bone, or throat pain; post-operative pain

muscle spasms or stiffness

feeling cold

feeling tired, drowsiness, or somnolence

burning, tingling/prickling sensation, decreased sensitivity, or feeling without stimulation

involuntary trembling movement

dehydration

decreased potassium level in the blood

mucosal inflammation

blood accumulation or inflammation in the nose, throat, or sinuses

upper respiratory tract infections such as a cold or urinary tract infections such as bladder infection

general infection

Herpes simplex (virus) infection

cough with sputum, wheezing, severe or labored shortness of breath

spitting blood or nosebleed

fluid in the pleural cavity

blood in urine, difficult or painful urination, or frequent urination

difficulty sleeping, depression, anxiety, or confusion

dizziness

tinnitus

blurred vision

hair loss

difficult and painful menstruation

hearing loss

decrease in white blood cell (leukocyte) count with or without fever, decrease in platelet count

Side effects with unknown frequency (cannot be estimated from the available data):

abnormal fluid accumulation around the heart (pericardial effusion)

If you experience any side effects not mentioned in these instructions for use, inform your doctor or pharmacist.

> **Reporting of side effects:**
> If any side effect, whether included in the Instructions for Use or not, occurs, talk to your doctor, pharmacist, or nurse. Also, you can report the side effects you encounter to the Turkish Pharmacovigilance Center (TÜFAM) by clicking on the "Drug Side Effect Notification" icon on www.titck.gov.tr or by calling the side effect notification line at 0 800 314 00 08. By reporting side effects, you will contribute to obtaining more information about the safety of the medicine you are using.

How to store MEPACT

Keep MEPACT out of the sight and reach of children and in its packaging.

Unopened vial

Store in a refrigerator (2 ° C – 8°C). Do not freeze.

Store the vial in the outer carton to protect it from light.

Prepared suspension

After preparing the suspension with sodium chloride 9 mg/mL (0.9%) solution, store at room temperature (approximately 20ºC - 25ºC) and use within 6 hours.

Do not use this medicine if you notice any visible signs of deterioration. Do not dispose of your medicine in wastewater. These measures will help protect the environment.

Do not throw away expired or unused medicines! Give them to the collection system specified by the Ministry of Environment and Urbanization.

THE FOLLOWING INFORMATION IS FOR HEALTHCARE PROFESSIONALS WHO WILL ADMINISTER MEPACT.

The following information is for medical or healthcare professionals only.

Instructions for preparing MEPACT for intravenous infusion

Materials included in each package:

1 vial of MEPACT (mifamurtide)

1 MEPACT filter

Materials required but not supplied with the product:

9 mg/mL (0.9%) sodium chloride solution for injection, 100 mL bag

1 disposable, 60 or 100 mL sterile Luer-lock syringe

2 sterile injection needles, medium (18) gauge

Reconstitution of the liposomal suspension is recommended to be performed in a laminar flow hood using sterile gloves and aseptic technique.

The lyophilized powder should be brought to approximately 20 °C – 25°C before reconstitution using the provided filter and diluent. This process takes approximately 30 minutes.

1. The vial cap should be removed, and the rubber stopper wiped with an alcohol pad.
2. The filter should be removed from its blister packaging, and the cap on the pointed end of the filter should be removed, then this pointed end should be immersed into the vial septum until it is fully seated. The Luer-lock cap of the syringe should not be removed at this time.
3. The 9 mg/mL (0.9%) sodium chloride solution for injection EP/USP in a 100 mL bag, needle, and syringe should be removed from their packaging (these are not included in the product packaging).
4. The area of the bag containing the 9 mg/mL (0.9%) sodium chloride solution for injection where the needle will be inserted should be wiped with an alcohol pad.

5. 50 mL of 9 mg/mL (0.9%) sodium chloride solution for injection should be drawn from the bag using a needle and syringe.

6. After detaching the needle from the syringe, the syringe should be attached to the filter by opening the Luer-lock cap on the filter (Figure 1).

Figure 1

7. The 9 mg/mL (0.9%) sodium chloride solution for injection should be added to the vial by gently and firmly pressing the plunger of the syringe. **The filter and syringe must not be separated from the vial.**

8. The vial should be left undisturbed for approximately 1 minute to allow complete hydration of the dry substance.

9. **Then, with the filter and syringe still attached to the vial, it should be shaken vigorously for 1 minute.** During this time, the liposomes form spontaneously (Figure 2).

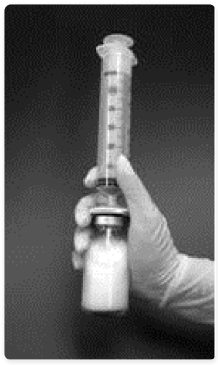

Figure 2

10. The desired dose can be withdrawn from the vial by inverting the vial and slowly pulling back the plunger of the syringe (Figure 3). Each milliliter of reconstituted suspension contains 0.08 mg of mifamurtide. The volume of suspension to be withdrawn from the vial to provide the desired dose is calculated as follows:

Volume of suspension to be withdrawn from vial = [12.5 x calculated dose (mg)] mL

For convenience, the following table can be used:

1 mg	12.5 mL
2 mg	25 mL
3 mg	37.5 mL

4 mg 50 mL

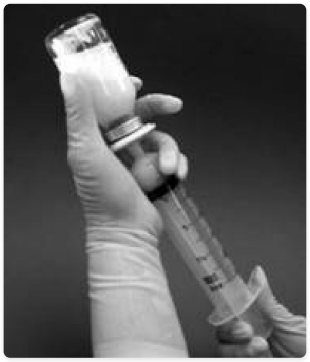

Figure 3

1. The syringe should then be detached from the filter, and a new needle attached to the syringe filled with the suspension. The injection site of the bag should be wiped with an alcohol pad, and the suspension in the syringe should be injected into the bag containing the remaining (50 mL) 9 mg/mL (0.9%) sodium chloride solution for injection (Figure 4).

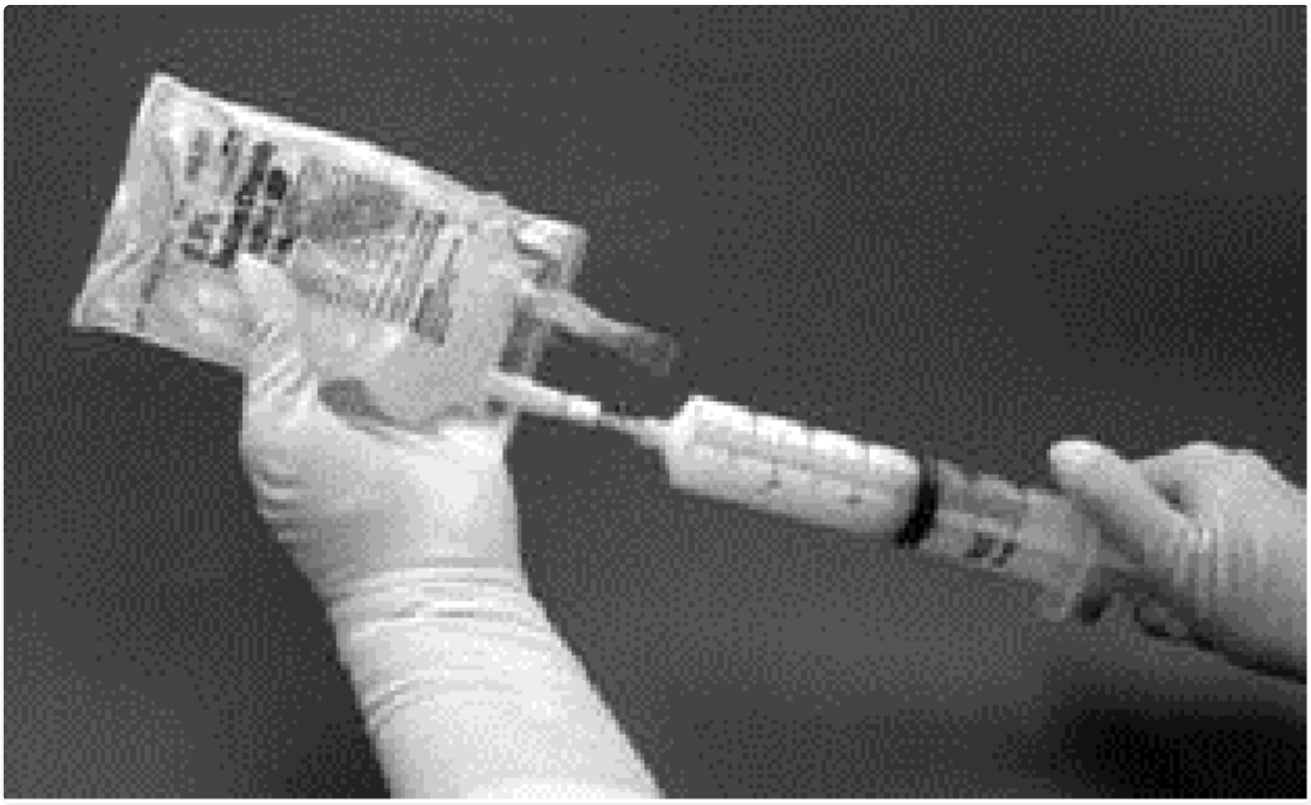

Figure 4

2. The bag should be gently inverted to mix the solution without excessive shaking.
3. The patient's identity and the date and time of administration should be written on the label of the bag containing the reconstituted and diluted liposomal suspension.
4. The suspension has been shown to be chemically and physically stable for 6 hours at room temperature (approximately 20º-25ºC).
5. From a microbiological point of view, it is recommended that the suspension be used immediately after preparation. If not used immediately, the storage times and conditions prior to use are the responsibility of the user and should not exceed 6 hours at room temperature (20º-25ºC).

6. The liposomal suspension should be administered as an infusion completed within one hour.

Disposal

Do not throw away expired or unused medicines! Give them to the collection system specified by the Ministry of Environment and Urbanization.

The waste from empty inner packaging after the use of cytotoxic and cytostatic medicinal products is**HAZARDOUS WASTE** and the management of this waste is carried out according to the Waste Management Regulation published in the Official Gazette dated 2/4/2015 and numbered 29314.

Marketing Authorization Holder:

Lucane Pharma Sağlık Hizmetleri Limited Şirketi Bakırköy/İstanbul

Manufacturer:

BSP Pharmaceuticals S.p.A. Via Appia Km 65,561 (loc. Latina Scalo) 04013 Latina (LT), Italy

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