PATIENT PACKAGE INSERT ACCORDING TO PHARMACISTS' REGULATIONS (PREPARATIONS) – 1986

The medicine is marketed with a doctor's prescription only

Navelbine® 20 mg
Soft Capsule

The active ingredient and its quantity:
Each soft capsule contains:
Vinorelbine (as tartrate) 20 mg

Navelbine® 30 mg
Soft Capsule

The active ingredient and its quantity:
Each soft capsule contains:
Vinorelbine (as tartrate) 30 mg

For a list of inactive and allergenic ingredients in the preparation, please see section 6 "Further Information" and section 2 "Important information about some of the ingredients of the medicine".

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

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

1. WHAT IS THE MEDICINE INTENDED FOR?

Navelbine is intended for the treatment of non-small cell lung cancer, treatment of advanced breast cancer.

Therapeutic group: Navelbine belongs to the group of medicines for the treatment of cancer extracted from the vinca plant (vinca alkaloids).

2. BEFORE USING THE MEDICINE

Do not use the medicine if:

- You are sensitive (allergic) to the active substance vinorelbine, or to any other substance from the family of cancer medicines called vinca alkaloids.
- You are sensitive (allergic) to any of the additional ingredients contained in Navelbine (for more information, please see section 6 "Further information" and section 2 "Important information about some of the ingredients of the medicine").
- You are pregnant or think that you are pregnant.
- You are breastfeeding.
- You suffer from a serious liver disease.
- You have had gastric or small intestine surgery or if you suffer from intestinal problems that affect the absorption of food. This may affect how Navelbine is absorbed in your body.
- Your white blood cell count (leukocytes, neutrophils) is low, or in the case of existing severe infection or occurring up to two weeks before taking the medicine.
- Your platelet count (thrombocytopenia) is low.
- You have recently received or are planning to receive a vaccine against yellow fever.
- You need long-term oxygen therapy.

In any case of doubt, consult the doctor or pharmacist.

Special warnings regarding use of the medicine

Before treatment with Navelbine, tell the doctor if:

- You have previously suffered from a heart attack or severe chest pain.
- Your ability to perform daily activities is strongly reduced.
- You have problems with your liver or have undergone radiotherapy where the treated area included the liver.
- Your doctor has told you that you have an intolerance to certain sugars; consult your doctor before taking this medicine.
- You show signs of infection (such as fever, chills, joint pain, cough).
- You take, or have recently taken, other medicines, including non-prescription medicines.
- You are planning to receive a vaccination or have recently received a vaccination.

Children and adolescents

The capsules are not recommended for treatment in children and adolescents under the age of 18 years.

Tests and follow-up

Blood cell count tests must be performed before and during the Navelbine treatment period, in order to make sure that it is safe for you to take the medicine. If the blood test results are abnormal, treatment may be delayed and further tests may need to be performed until your blood test results show normal values.

Drug interactions

If you are taking, or have recently taken, other medicines, including non-prescription medicines and nutritional supplements, inform the doctor or pharmacist. If you are given Navelbine as well as medicines that affect your bone marrow it may make some of the side effects worse. In particular, tell the doctor or pharmacist if you are taking:

Your doctor should take note if you are taking any of the following medicines:

- Medicines to thin your blood (anticoagulants)
- A medicine to treat epilepsy, called phenytoin
- Antifungal medicines, such as itraconazole and ketoconazole
- An anti-cancer medicine called mitomycin C
- Immunosuppressants such as cyclosporin and tacrolimus

Many vaccines (live attenuated vaccine) are not recommended during treatment. Inform your doctor if you are required to get vaccinations.

Use of the medicine and food

The Navelbine capsule should be swallowed whole with water without chewing or sucking the capsule. It is advisable to take the medicine together with a light meal. Do not drink a hot beverage with the medicine, as it may cause the capsule to dissolve too quickly.

Pregnancy, breastfeeding and fertility

Fertility

Fertility in men: If you are being treated with Navelbine, the advice to you is not to father a child during treatment and for 4 months after taking the last capsule.

Consult your doctor about sperm preservation before starting treatment because Navelbine may alter your fertility. You must use an effective contraception during treatment and for 4 months after the end of treatment.

Women of child-bearing potential: If you are a woman of child-bearing potential, you must use an effective contraception (birth control) during treatment and for 7 months after the end of treatment.

Pregnancy

Do not take Navelbine if you are pregnant or think that you are pregnant. If you must start treatment with Navelbine and you are pregnant, or in the case of becoming pregnant during treatment with the medicine, do not stop taking the medicine. Refer to a doctor immediately and ask him about any potential risks for the unborn child.

Breastfeeding

Do not take Navelbine if you are breastfeeding. Stop breastfeeding if treatment with Navelbine is necessary.

Consult a doctor or pharmacist before taking medicines.

Driving and using machines

It is unlikely that Navelbine treatment will affect your ability to drive or operate machinery. However, some of the side effects of Navelbine may affect your ability to drive or operate machinery. See section 4 **"Side effects"** for details. Therefore, it is recommended not to drive if you feel unwell or if your doctor has advised you to avoid driving.

Important information about some of the ingredients of the medicine

The medicine contains sorbitol, alcohol and sodium.

If the doctor has told you that you have an intolerance to certain sugars, consult the doctor before taking the medicine.

Navelbine 20 mg contains 5.36 mg of sorbitol in each capsule.

Navelbine 30 mg contains 8.11 mg of sorbitol in each capsule.

Navelbine 20 mg contains 5 mg of alcohol (ethanol) in each capsule.

Navelbine 30 mg contains 7.5 mg of alcohol (ethanol) in each capsule.

The amount of alcohol in each capsule of this medicine (Navelbine 20 mg, Navelbine 30 mg) is equal to less than 1 ml of beer or 1 ml of wine. The little amount of alcohol in this medicine will not have noticeable effects.

This medicine (Navelbine 20 mg, Navelbine 30 mg) contains less than 23 mg of sodium per capsule, and is therefore considered "sodium-free".

3. HOW SHOULD YOU USE THE MEDICINE?

Navelbine should be given under the medical supervision of a qualified physician experienced in cancer treatment.

The medicine is intended for oral use.

Always use the preparation according to the doctor's instructions. You should check with the doctor or pharmacist if you are not sure about the dosage and treatment regimen of the preparation.

The dosage and treatment regimen will be determined by the doctor only. Before and during treatment with Navelbine, your doctor will check your blood cell count to determine when you will receive the treatment and which dose is suitable for you. Your doctor will tell you the number and strength of capsules you will need to take each week. This will be determined according to your body weight and height.

Your doctor will calculate your body surface area in square meters (m^2). The usual weekly dose is taken in a single dose and calculated at 60 mg per square meter of your body's surface area for the first 3 doses of treatment. After the third dose, your doctor will decide whether to increase the dosage and calculate the dose at 80 mg per square meter of your body's surface area. In any case, your doctor may adjust the dose of Navelbine.

If you receive the Navelbine capsules with another medicine to treat your medical condition, your doctor will decide what the appropriate dose will be for you.

Do not exceed a total dose of 160 mg per week.
Do not take Navelbine more than once a week.

Frequency of administration of the medicine

Navelbine is usually administered once a week. The frequency of administration will be determined by your doctor.

The preparation is cytotoxic.
Do not exceed the recommended dose.

Duration of treatment

The duration of treatment will be determined by your doctor.

If you take an anti-nausea/vomiting medicine

Navelbine can cause vomiting: see section 4 **"Side effects"**. If your doctor has prescribed you an anti-sickness medicine, take this medicine according to the doctor's instructions.

Taking Navelbine with a light meal can help to reduce the feeling of nausea.

Method of administration of the medicine

Before opening the blister (tray) containing Navelbine, make sure that the capsule is not damaged because the liquid inside the capsule causes irritation and may be harmful if it comes into contact with your skin, eyes or mucosa. If contact occurs, wash the affected area **immediately** and thoroughly with water.

Do not swallow a damaged capsule: return it to your doctor or pharmacist.

Instructions for opening the blister package (tray):

1. Cut the blister along the marked line (black dotted line) with a pair of scissors.
2. Peel the soft plastic foil off.
3. Push the capsule through the aluminum foil.

Using the medicine

- Swallow the capsule whole with water; it is preferable to take the medicine with a light meal. Do not drink a hot beverage with the medicine, as it may cause the capsule to dissolve too quickly.
- **Do not** chew or suck the capsule.
- If you chew or suck a capsule by mistake, rinse your mouth thoroughly with water and contact your doctor **immediately**.
- If you vomit within a few hours after taking the medicine, contact your doctor; **do not repeat administration of the same dose.**

If you have accidentally taken a higher dosage

If you have taken more Navelbine than the dose the doctor prescribed, refer to a doctor **immediately**. Your dose of Navelbine is carefully monitored and checked by your doctor and pharmacist; however, even if you have received the right dose of chemotherapy, your body may still respond with severe symptoms. Some of the symptoms may develop as signs of an infection (such as fever, chills, cough, joint pain). Severe constipation may also develop. If these severe symptoms occur, immediately refer to a doctor.

If you have taken an overdose or if a child has accidentally swallowed the medicine, refer to a doctor or hospital emergency room immediately and bring the medicine package with you.

If you forgot to take the medicine

Do not take a double dose to make up for the forgotten dose. Refer to your doctor who will set a new time for taking the dose.

Adhere to the treatment regimen as recommended by the doctor.

If you stop taking the medicine

Your doctor will decide when to stop the treatment. However, if you want to stop the treatment earlier, you should consult your doctor about other options.

Do not take medicines in the dark! Check the label and the dose each time you take a medicine. Wear glasses if you need them.

If you have further questions regarding the use of the medicine, consult the doctor or pharmacist.

4. SIDE EFFECTS

As with any medicine, use of Navelbine 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.

Contact the doctor immediately if you experience any of the following symptoms during treatment with Navelbine:

- A chest pain, breathlessness and fainting, which can be symptoms of a clot in a blood vessel in the lungs (pulmonary embolism).
- Headaches, changed mental state which may lead to confusion and coma, convulsion, blurred vision and high blood pressure, which could be sign of a neurological disorder such as posterior reversible encephalopathy syndrome.
- Cough, fever and chills that can be signs of a severe infection or generalized infection (septicemia), which can be serious.
- Severe constipation with abdominal pain, without bowel emptying for several days.
- Severe dizziness or lightheadedness upon standing up, a sign of a severe drop in blood pressure.
- Severe chest pain which is not normal for you. The symptom may be due to a disturbance in the heart function due to insufficient blood flow, called a heart attack (may sometimes be fatal).
- Breathing difficulty, rash spread over the whole body, swelling of the eyelids, lips or throat, which may be signs of an allergic reaction.

Very common side effects (effects that occur in more than one out of ten users)

Infections in different areas; Disorders of the digestive system; Diarrhea, constipation, abdominal pain, nausea and vomiting; Inflammation of the mouth; Decrease in red blood cell count which may cause paleness, weakness or shortness of breath; A decrease in the platelet count that may increase the risk of bleeding or bruising; A decrease in the white blood cell count, which makes you more vulnerable to infections; Loss of some reflex reactions, sometimes a change in the sense of touch; Hair loss, usually moderate; Tiredness; Fever; Feeling of discomfort; Weight loss, loss of appetite

Common side effects (effects that occur in 1-10 users out of 100)

Difficulties in coordinating muscle movement; Vision changes; Shortness of breath, cough; Difficulty urinating; Additional symptoms in the genitourinary system; Sleeping difficulties; Headache; dizziness; Change in the sense of taste; Pharyngitis, difficulty in swallowing food or liquids; Skin reactions; Chills; Weight gain; Joint pain, jaw pain, muscle pain; Pain in different body parts and in the tumor area; High blood pressure; Liver disorders (abnormal results of liver tests)

Uncommon side effects (effects that occur in 1-10 users out of 1000)

Heart failure which may be manifested by shortness of breath and swelling of the ankles, irregular heartbeats; Lack of muscle control, may be manifested in abnormal gait, changes in speech and unusual eye movements (ataxia)

Side effects of unknown frequency (effects whose frequency has not yet been determined)

Blood infection (sepsis), manifests in symptoms such as high fever and deterioration of general health; Heart attack (myocardial infarction); Gastrointestinal bleeding; Decreased amount of blood sodium, and in some cases may be the result of an overproduction of a hormone that causes fluid retention, and may manifest itself in symptoms such as weakness, muscle cramps, fatigue, confusion or unconsciousness (SIADH – Syndrome of Inappropriate Antidiuretic Hormone secretion)

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

Reporting side effects

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
Additionally, you can report to Padagis via the following address: www.Padagis.co.il

5. HOW TO STORE THE MEDICINE?

- Avoid poisoning! This medicine and any other medicine must be stored in a closed 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 and blister (tray). The expiry date refers to the last day of that month.
- Store in a refrigerator (2°C-8°C). Store in the original package.
- Do not dispose of medicines in wastewater or household waste. For safety reasons, unused capsules must be returned to your doctor or pharmacist for disposal. Taking these measures will help protect the environment.

6. FURTHER INFORMATION

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

Macrogol 400; Gelatine; Glycerol 85%; Purified water; Dry substance of ANIDRISORB 85/70 (sorbitol, sorbitan-1.4, superior polyols, mannitol); Ethanol anhydrous; Glycerol; Titanium dioxide E171; Yellow iron oxide E172 (in Navelbine 20mg); Red iron oxide E172 (in Navelbine 30mg); Triglycerides, Medium chain; Triglycerides Medium chain and Phosal 53 MCT (standardized phosphatidylcholine concentrate);

Edible printing ink: E120, Hypromellose, Propylene glycol.

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

Navelbine 20 mg: a light brown, soft capsule containing light yellow to orange-yellow liquid, on which N20 is printed in red. The package contains one capsule in a blister (tray).

Navelbine 30 mg: a pink, soft capsule containing light yellow to orange-yellow liquid, on which N30 is printed in red. The package contains one capsule in a blister (tray).

- Registration holder, importer and its address: Padagis Israel Agencies Ltd., 1 Rakefet St., Shoham.
- Revised in October 2023 according to MOH guidelines.
- Registration number of the medicine in the National Drug Registry of the Ministry of Health:
  Navelbine 20 mg: 130-90-30910
  Navelbine 30 mg: 130-91-30911

NAVELBINE is a registered trademark of Pierre Fabre Medicament

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