PACKAE LEAFLET: INFORMATION FOR THE USER
Vinorelbine "Ebewe" 10 mg/ml – Concentrate for solution for infusion

Each 1 ml concentrate for solution for infusion contains 10mg Vinorelbine (as tartrate)
Each 5ml concentrate for solution for infusion contains 50mg Vinorelbine (as tartrate)

Read all of this leaflet carefully before you start taking this medicine because it contains important information for you.
- Keep this leaflet. You may need to read it again.
- If you have further questions, please ask your doctor or nurse.
- If you get any side effects, talk to your doctor or nurse. This includes any possible side effects not listed in this leaflet. See section 4.

What is in this leaflet:

1. WHAT VINORELBINE IS AND WHAT IT IS USED FOR
Vinorelbine belongs to a family of medicines used to treat cancer called the vinca-alkaloid family. It can be used alone but more commonly it is used in combination with other anti-cancer agents. Vinorelbine can also be used in advanced breast cancer and non-small cell lung cancer.

2. WHAT YOU NEED TO KNOW BEFORE YOU TAKE VINORELBINE
You will not be given Vinorelbine if you:
- are allergic (hypersensitive) to Vinorelbine or any of the other ingredients of Vinorelbine (see section 6 in this leaflet).
- are under 18 years of age,
- you have a low white blood cell (neutrophils, leucocyte) count or a severe infection current or recent (within 2 weeks),
- If you have a low platelet count (thrombocytopenia),
- If you plan to receive a yellow fever vaccination or have just received one

Warnings and precautions:
Talk to your doctor or nurse before using Vinorelbine, you should tell your doctor pharmacist if:

- you have a history of heart attack or severe chest pain,
- you have problems with your liver or you have received radiotherapy where the treatment field included the liver,
- you have signs or symptoms of infection (such as fever, chills, joint pain, cough),
- you take or have recently taken any other medicines including medicines obtained without prescription,
- you plan to have a vaccination or have just had one,
- you are Japanese, as there is a higher report of lung disease affecting the tissue and space around the air sacs of the lungs in this population,
- Before and during your treatment with vinorelbine, blood cell counts are performed to check that it is safe for you to receive treatment. If the results of this analysis are not satisfactory, your treatment may be delayed and further checks made until these values return to normal.

Children and adolescents
Vinorelbine is not recommended for use by children younger than 18 years

Other medicines and vinorelbine:
Please tell your doctor or pharmacist if you are taking or have recently taken any other medicines, including medicines obtained without a prescription.

Your doctor should take special attention if you are taking the following medicines:

- medicines used to thin your blood (anticoagulants),
- an anti-epileptic medicine called phenytoin,
- antifungal medicines such as itraconazole and ketaconazole,
- medicines to treat HIV such as ritonavir,
- medicines to treat high blood pressure called verapamil,
- medicines to treat irregular heart rhythm conditions such as quinidine
- medicines for epilepsy such as carbamazepine,
- medicines for treating mood such as St. John's Wort (Hypericum perforatum)
- anti-cancer medicines called mitomycin C, or cisplatin. There is an increased risk of difficulty breathing if Vinorelbine is used with mitomycin C.
- medicines that decrease the activity of your immune system such as ciclosporin and tacrolimus.
- some antibiotics such as clarithromycin, erythromycin, telithromycin and rifampicin
- some sedatives (barbiturates): phenobarbital.

Many vaccines (live attenuated vaccines) are not recommended during treatment. Please inform your doctor if you require any vaccinations.

Pregnancy, breast-feeding and fertility
Pregnancy
Vinorelbine should not be given to pregnant women, because it can cause serious birth defects. If you are a woman of child-bearing age you should take contraceptives (birth control) to prevent becoming pregnant during and for at least 3 months after treatment with Vinorelbine.

If you should become pregnant during treatment you should immediately contact your doctor for advice. Genetic counselling is recommended.
If you are planning to become pregnant, you must contact your doctor or health care provider to discuss the potential adverse effects.

Breast-feeding
Breast-feeding should be discontinued if treatment is necessary as it is not known whether it might pass into breast milk thereby affecting the baby.

Male fertility
Men being treated with vinorelbine are advised not to father a child during treatment and for up to 3 months after the end of the treatment and to seek advice on conservation of sperm prior to treatment because vinorelbine may alter male fertility.

Driving and using machines:
No studies on the effects on the ability to drive and use machines have been performed.
However, some of the possible side effects of vinorelbine could affect your ability to drive or perform skilled tasks: see section 4; Possible side effects below for details. Therefore, it is recommended that you should not drive if you feel unwell or if your doctor has advised you not to drive.

3. HOW TO TAKE VINORELBINE

This drug will be given to you under the supervision of medical personnel. The dosage of vinorelbine will depend on the condition you are being treated for, your response to the therapy and other medication you are being given. If you notice any unusual signs, symptoms or sensations please notify your doctor or pharmacist immediately as your general condition and your response to the treatment will be closely monitored before, during and after treatment.

If you take more Vinorelbine than you should:
As this drug is given to you whilst in hospital it is unlikely that you will be given too much or too little, however if overdose occurs or you feel marked side effects tell your doctor immediately.

4. POSSIBLE SIDE EFFECTS
Like all medicines, this medicine can cause side effects, although not everybody gets them. Your doctor will discuss these with you and will explain the potential risks and benefits of your treatment.

If you get any of the following symptoms you should contact your doctor immediately:

- signs of a major infection such as cough, fever and chills,
- severe constipation with abdominal pain when your bowels have not been open for several days,
- severe dizziness, light-headedness when you stand up,
- severe chest pain which is not normal for you,
- signs of allergy such as itching, shortness of breath.

Between infusions of Vinorelbine the following side-effects may occur:

Very common (experienced in 1 in 10 patients)
- decrease in the number of red blood (anaemia), or white blood cells
- loss of some reflex reactions, occasionally difference in the perception of touch
- weakness of the lower extremities
- feeling sick (nausea), vomiting
- inflammation of the linings of the mouth or the throat
- raised liver enzymes
- hair loss
- at the site of injection: pain, inflammation of the vein, skin discolouration, redness of the skin

Common (experienced in less than 1 in 10 but more than 1 in 100 patients)
- infections
- decrease in the number of platelets (may causing unusual bleeding or bruising)
- diarrhoea
- inflammation of the lining the tube that carries food from the throat to the stomach (oesophagitis)
- tiredness (asthenia, fatigue)
- fever
- pain at different sites around the body, chest pain, back pain, pain where the tumor is
- joint pain (arthralgia), jaw pain, muscle pain (myalgia)
- tests showing an increased level of creatinine in the body, indicating your kidneys may not be working as well as they should

Uncommon (experienced in less than 1 in 100 but more than 1 in 1000 patients)
- severe signs of a major infection such as cough, fever chills and blood infection
- severe difficulties with your body movements and sense of touch (severe paresthesias)
- reduced blood pressure (hypotension with symptoms such as dizziness or feeling faint)
- raised blood pressure (hypertension) with symptom such as a headache

- sudden feelings of heat and skin redness of the face and neck (flushing)
- feeling cold in the hands and feet (peripheral coldness)
- difficulty in breathing or wheezing (dyspnoea and bronchospasm)

Rare (experienced in less than 1 in 1000 but more than 1 in 10,000)
- breathing difficulties – if you are receiving another cancer drug called mitomycin C
- paralysis of the gut
- inflammation of the pancreas
- skin rashes
- ulcer at the injection site (local necrosis)
- low blood sodium (leading to tiredness, confusion, muscle twitching and coma)
- chest pain, heart attack (ischaemic heart disease, angina pectoris, myocardial infarction)
- severe drop in blood pressure
- constipation

Very rare (experienced in less than 1 in 10,000 patients)
- irregular heart beat
- life treating infections
- nervous system disorder causing muscle weakness, loss of reflexes, and numbness or tingling in your arms, legs, face, and other parts of your body (Guillain Barre Syndrome)

Not known (cannot be evaluated from existing data)
Other side effects have been reported with a "not known" frequency:
- Generalised allergic reactions. These are serious reactions which can cause severe difficulty in breathing, dizziness, rash affecting your whole body, swelling of the eyelids, face lips, throat (anaphylactic shock, anaphylaxis, anaphylactoid type reactions).
- A fall in white blood cell count with fever (febrile neutropenia), a general infection in combination with a fall in white blood cell count (neutropenic sepsis).
- Low sodium level due to an overproduction of a hormone causing fluid retention and resulting in weakness, tiredness or confusion (Syndrome of Inappropriate Antidiuretic Hormone secretion SIADH).
- Loss of appetite (anorexia).
- Skin redness (erythema) on the hands and feet.

Reporting of side effects
If you get any side effects, talk to your doctor, pharmacist or nurse. This includes any possible side effects not listed in this leaflet. You can also report side effects directly via HPRA Pharmacovigilance, Earlsfort Terrace, IRL - Dublin 2; Tel: +353 1 6764971; Fax: +353 1 6762517. Website: http://www.hpra.ie; E-mail: medsafety@hpra.ie.

By reporting side effects you can help provide more information on the safety of this medicine.

5. HOW TO STORE VINORELBINE
Keep this medicine out of the sight and reach of children.

Do not use this medicine after the expiry date which is stated on the label after EXP:
The expiry date refers to the last day of that month.

Store in a refrigerator (2 - 8 °C). Keep the vials in the outer carton

For single use only. Discard any unused contents.
The product should be used immediately after opening.

Details on the in-use stability of the diluted product are included in the section of the leaflet for medical or healthcare professionals.

Do not use Vinorelbine if you notice any visible signs of deterioration.

Please ensure disposal of any un-used product in line with the local guidelines for cytotoxic material disposal.

6. CONTENTS OF THE PACK AND OTHER INFORMATION

What Vinorelbine "Ebewe" 10 mg/ml – Concentrate for solution for infusion contains:
The active substance is Vinorelbine (as Vinorelbine Tartrate).
Each 1ml vial contains 10mg of Vinorelbine (as Vinorelbine Tartrate).
Each 5ml vial contains 50mg of Vinorelbine (as Vinorelbine Tartrate)
The other ingredient is Water for Injection.

What "Ebewe" 10 mg/ml – Concentrate for solution for infusion looks like and contents of the pack:
Concentrate for solution for infusion is a clear, colourless to pale yellow solution packed in glass vial with a stopper is covered with a crimped-on aluminium cap equipped with a polypropylene flip-off cap.

Pack sizes: 1ml & 5ml vials packed in single cartons

Not all vial sizes may be marketed.

Marketing Authorisation Holder and Manufacture

Marketing Authorisation Holder
Fannin Limited
Fannin House
South County Business Park
Leopardstown
Dublin 18
Ireland

Manufacturer:
EBEWE Pharma Ges.m.b.H. Nfg. KG
A-4866 Unterach, AUSTRIA

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THE FOLLOWING INFORMATION IS INTENDED FOR MEDICAL OR HEALTHCARE PROFESSIONALS ONLY:

INSTRUCTIONS FOR USE AND HANDLING AND DISPOSAL
Strictly intravenous administration after appropriate dilution.
Intrathecal administration of Vinorelbine® may be fatal.

Before application it is extremely important to ensure that the intravenous needle is positioned in the vein. Leakage into surrounding tissue during administration of vinorelbine may cause considerable irritation. If extravasation occurs, the injection should be discontinued immediately, and any remaining portion of the dose should then be introduced into another vein.
It is recommended to infuse Vinorelbine® over 6-10 minutes after dilution in 20-50 ml of sodium chloride 9 mg/ml (0.9%) solution for injection or in glucose solution for injection 5%.

Administration should always be followed with at least 250 ml of an isotonic solution infusion to flush the vein. (See section 4.2 of the Summary of Product Characteristics for more information)

After Dilution:
The product should be used immediately after opening

Chemical and physical in-use stability has been demonstrated for 25 days when stored in a refrigerator (at 2-5°C) or at room temperature and protected from light. Chemical and physical in-use stability has been demonstrated for 4 days when stored at room temperature without protection from light. See section 6.6 for the compatible diluents.
From a microbiological point of view, the product should be used immediately. If not used immediately, in-use storage times and conditions prior to use are the responsibility of the user and would normally not be longer than 24 hours at 2 to 5°C, unless reconstitution/dilution has taken place in controlled and validated aseptic conditions

The diluted solution for infusion is a clear, colourless or pale yellow solution.
Vinorelbine neither reacts with plastic nor with neutral colourless glass.

Handling guidelines:
The preparation and administration of vinorelbine should be carried out by trained staff and as with all cytotoxic agents; precautions should be taken to avoid exposing staff during pregnancy. Preparation of solution for administration should be carried out in a designated handling area and working over a washable tray or disposable plastic-backed absorbent paper.Suitable eye protection, disposable gloves, face mask and disposable apron should be worn. Eventual spillage or leakage should be mopped up.

Care must be taken to avoid product contamination of the eye thereby causing severe irritation or even corneal ulcer. If exposure occurs, the eyes should immediately be thoroughly flushed with physiologic sodium chloride 9 mg/ml (0.9%) solution for 15 minutes. On completion, any exposed surface should be thoroughly cleaned and hands and face washed**.**

Extravasation
It is advisable to give the drug via the tubing of a freely-running I.V. Saline infusion after checking that the needle is well placed in the vein. This method minimises the risk of drug extravasation and makes sure that the vein is flushed with saline after the administration of the drug. Extravasation of Vinorelbine from the vein during injection may give rise to severe tissue lesions, even necrosis. Venous sclerosis may result from injection into small vessels or repeated injections into the same vein. Infusion preparations are to be prepared either with 0.9 % sodium chloride or with 5 % glucose. If extravasation occurs, the injection should be discontinued immediately, and any remaining portion of the dose should then be introduced into another vein

Incompatibilities
Vinorelbine concentrate for solution for infusion must not be mixed with other preparations except with those mentioned in section 6.6 of the Summary of Product Characteristics
Vinorelbine concentrate for solution for infusion must not be diluted with alkaline solutions due to the risk of precipitation. In case of polychemotherapy Vinorelbine “Ebewe” should not be mixed with other agents.
Vinorelbine “Ebewe” is not absorbed to or affected by PVC, PE or clear neutral glass.
Any unused product or waste material should be disposed of in accordance with local requirements.