PACKAGE LEAFLET: INFORMATION FOR THE USER

Vinorelbine 10 mg/ml concentrate for solution for infusion

Vinorelbine

Read all of this leaflet carefully before you start using this medicine.
- Keep this leaflet. You may need to read it again.
- If you have any further questions, ask your doctor or pharmacist.
- This medicine has been prescribed for you. Do not pass it on to others. It may harm them, even if their symptoms are the same as yours.
- If any of the side effects gets serious, or if you notice any side effects not listed in this leaflet, please tell your doctor.

In this leaflet:

1. WHAT VINORELBINE IS AND WHAT IT IS USED FOR

Vinorelbine is used in the treatment of cancer and belongs to a group of medicines known as Vinca alkaloids.
Vinorelbine is used to treat certain types of lung cancer and breast cancer.

2. BEFORE YOU USE VINORELBINE

Do not use Vinorelbine
- if you are allergic (hypersensitive) to vinorelbine, other Vinca alkaloids, or any of the other ingredients of this medicine (see section 6).
- if you have or recently had serious infection or severe decrease in white blood cells (neutropenia)
- if you have severe decrease in blood platelets.
- if you are pregnant
- if you are breast-feeding (breast-feeding should be discontinued during treatment with vinorelbine)
- if you are a women of childbearing potential not using effective contraception
- in combination with yellow fever vaccine

This medicine is strictly for intravenous use only and should not be injected into the spine.

Take special care with Vinorelbine

- if you have had a heart disease involving lack of blood supply to the heart (ischaemic heart disease, angina)
- if you are having radiotherapy and the treatment field includes the liver
- if you present signs or symptoms suggestive of infection (such as fever, chills, sore throat), let your doctor know immediately, so that he/she can carry out any tests which may be needed
- if you have impaired liver function
- if you have had a vaccination recently or need a vaccination. Special care must be taken with live attenuated vaccines as measles, mumps, rubella, polio, varicella and tuberculosis (BCG)
- if you receive a cancer medicine named mitomycin C, phenytoin, itraconazole, or any other medicine mentioned in the section "Using other medecines."

Vinorelbine must not get into contact with the eye as there is a risk of severe irritation and even corneal ulceration. If this occurs, immediately rinse the eye with normal saline solution and contact an ophthalmologist.

Men and women who are treated with Vinorelbine should use an effective contraception during treatment and after treatment; please refer to the section on pregnancy and breastfeeding. Men and women should BOTH read the information under pregnancy and breast-feeding below.

Before each administration of Vinorelbine, a blood sample will be taken for analysis of its components. If the results of this analysis are not satisfactory, your treatment may be delayed and further checks made until these values return to normal.

Using other medicines
Please tell your doctor if you are taking or have recently taken any other medicines, including medicines obtained without a prescription. This is especially important if you are using any of the following medicines:

- other medicines which can affect the bone marrow e.g. anti-cancer medicines
- carbamazepine, phenytoin and phenobarbital (medicines for the treatment of epilepsy)
- antibiotics such as rifampicin, erythromycin, clarithromycin, telithromycin
- St John's Wort (*Hypericum perforatum*)
- ketoconazole and itraconazole (medicines for the treatment of fungal infections)
- antiviral medicines to treat HIV-infection e.g. ritonavir (HIV protease inhibitors).
- nefazodon (medicines for the treatment of depression)
- cyclosporine and tacrolimus (medicine which decrease the activity of the immune system)
- verapamil, quinidine (medicines for the treatment of heart diseases)
- other medicines for the treatment of cancer e.g. mitomycin C, cisplatin. There is an increased risk of difficulty breathing if Vinorelbine is used with mitomycin C.
- blood thinning medicines e.g. warfarin
- vaccines (see "Take special care with Vinorelbine).

Pregnancy and breast-feeding

Vinorelbine should not be given to pregnant women, because it can cause serious birth defects.

If you are a woman of childbearing age you must use an effective method of contraception during treatment and for up to 3 months after the end of the treatment. If pregnancy occurs during your treatment you must immediately inform your doctor. If you are or become pregnant during treatment with Vinorelbine, genetic counselling is recommended.

If you are a man, you should avoid fathering a child during treatment with Vinorelbine and for 6 months after treatment has stopped. There is also a risk that treatment with Vinorelbine will lead to male infertility and you may wish to seek advice about sperm storage before the treatment starts.

You must discontinue breast-feeding before treatment with Vinorelbine starts as it is not known whether it might pass into breast milk thereby affecting the baby.

Ask your doctor or pharmacist for advice before taking any medicine.

Driving and using machines
No studies on the effects on the ability to drive have been performed but no negative influence is expected. However, caution is necessary in patient treated with vinorelbine considering some adverse effects of the drug. Do not drive or use machines if you feel drowsy, or if you experience any other effect which may impair your ability to drive or use machines.

3. HOW TO USE VINORELBINE

Vinorelbine will be given to you under the supervision of a doctor specialized in this type of treatment.
The dosage depends on the condition you are being treated for, your response to the therapy and other medication you are being given. Your general condition and your response to the treatment will be closely observed before, during and after the vinorelbine treatment.

The usual dosage of vinorelbine is 25-30mg/m^2 of body surface area given once a week.

The medicine should be diluted before use with a solution of sodium chloride or glucose and given into a vein as an injection over 6-10 minutes or by infusion (drip) over 20-30 minutes. Following your treatment, a solution of sodium chloride will be used to flush the vein.

Dosage may be reduced if you have severe liver problems.

The safety and efficacy in children have not been determined.

If you use more Vinorelbine than you should
As this medicine will be given to you whilst you are in hospital it is unlikely that you will be given too little or too much, however, tell your doctor or pharmacist if you have any concerns.

4. POSSIBLE SIDE EFFECTS

Like all medicines, Vinorelbine can cause side effects, although not everybody gets them.

Frequency:
Very common: affects more than 1 user in 10.
Common: affects 1 to 10 users in 100
Uncommon: affects 1 to 10 users in 1,000
Rare: affects 1 to 10 users in 10,000
Very rare: affects less than 1 user in 10,000
Not known: frequency cannot be estimated from the available data.

Serious side effects – if any of the following side effects occur, immediately contact your doctor:
*Common:*chest pain.

Uncommon: Narrowing of the airways (bronchospasm), shortness of breath

Rare: Angina pectoris (pain in the chest radiating into the neck or arm). Heart attack, lung disease.

*Very rare:*complicated septicaemia (blood poisoning)

Not known: Acute systemic allergic reaction (anaphylaxis, anaphylactic shock)

These are very serious side effects. You may need immediate medical care.

Other side effects – if any of the following side effects occur, contact your doctor as soon as possible:
Very common: Low count of white blood cells, which may increase the risk of infection. Low count of red blood cells (anaemia), which may make you feel tired. Inflammation of the mouth or the gullet. Nausea and vomiting. Constipation and diarrhoea. Hair loss. Oedema, tenderness, pain and/or rash on the injection site. Abnormal results of liver function tests, loss of deep tendon reflexes. Weakness of lower extremities.

Common: Joint, muscle and jaw pain. Increased creatinine values (change in renal function). Symptoms of infection e.g. fever, pain. Low count of blood platelets (risk of bleeding). Fatigue, fever, weakness, pain at different locations including pain at the tumour site.

Uncommon: severe sepsis (blood infection). Numbness (paraesthesia). High blood pressure, low blood pressure, flushing and peripheral coldness.

Rare: Inflammation of the pancreas, paralytic intestinal blockage (ileus). Low levels of sodium in the blood. Injection site necrosis. Collapse due to low blood pressure.

Very rare: Guillain-Barrés syndrome (inflammation in peripheral nerves which may cause weakness). Heart rhythm disorders.

Not known: A reduction in a special type of white blood cells, which can result in fever. Syndrome of Inappropriate Antidiuretic Hormone Secretion (SIADH syndrome). Symptoms of this include increased weight, nausea (feeling sick), vomiting, muscle cramps, confusion and seizures (fits). Anorexia (decreased appetite). Skin reactions.

As changes in the blood may occur, your doctor may order blood samples to be taken to control this (low count of white blood cells, anaemia and/or low count of blood platelets, influence on the liver- or kidney function and the electrolyte balance in your body).

If any of the side effects gets serious, or if you notice any side effects not listed in this leaflet, please tell your doctor or pharmacist.

5. HOW TO STORE VINORELBINE

Keep out of the reach and sight of children.

Do not use Vinorelbine after the expiry date which is stated on the label and carton after EXP. The expiry date refers to the last day of that month.

Do not use Vinorelbine if any particulate contamination is noticed.

Unopened:
Store in a refrigerator (2°C – 8°C).
Keep the vial in the outer carton in order to protect from light.

After opening:
The content of the vial should be used immediately after the first opening of the vial.

After dilution:
Following dilution with physiological sodium chloride solution or 50 mg/mL (5%) glucose solution, the chemical and physical stability of the reconstituted solution has been confirmed for 24 hours at 2 – 8°C and not above 25°C at concentrations from 0.5 mg/ml to 3.0 mg/ml.

From a microbiological point of view the product should be used immediately. If not used immediately, in-use storage times and conditions are the responsibility of the user and would normally not be longer than 24 hours at 2-8°C, unless dilution has taken place in controlled and validated aseptic conditions.

Medicines should not be disposed of via wastewater or household waste. Ask your pharmacist how to dispose of medicines no longer required. These measures will help to protect the environment.

6. FURTHER INFORMATION

What Vinorelbine contains
The active substance is vinorelbine. One ml concentrate for solution for infusion contains 10 mg vinorelbine equivalent to 13.85 mg vinorelbine tartrate.
Each 1ml vial contains 10mg of vinorelbine (as tartrate).
Each 5ml vial contains 50mg of vinorelbine (as tartrate).
The other ingredient is water for injections.

What Vinorelbine looks like and contents of the pack
Vinorelbine 10mg/ml Concentrate For Solution For Infusion is a clear, colourless to slightly yellow solution in a colourless glass vial (type I), with a grey bromobutyl rubber stopper and sealed with a light blue flip off aluminium seal.

Pack-sizes:
1 x 1ml vial
1 x 5ml vial

Not all pack sizes may be marketed.

Marketing Authorisation Holder
Generics [UK] Limited
Station close, Potters Bar,
Hertfordshire EN6 1TL
United Kingdom

Manufacturers
Strides Arcolab Polska Sp.z.o.o.
10, Daniszewska Str
03-230 Warsaw
Poland

This medicinal product is authorized in the Member States of the EEA under following names:

This leaflet was last approved in

The following information is intended for medical or healthcare professionals only:

Vinorelbine 10mg/ml Concentrate For Solution For Infusion

Instruction for use

ANTINEOPLASTIC AGENT

Please refer to the Summary of Product Characteristics for detailed information regarding this product.

Handling and use
The preparation and administration of injectable solutions of cytotoxic agents must be carried out by trained specialist personnel with knowledge of the medicines used, in conditions that guarantee the protection of the environment and, in particular, the protection of the personnel handling the medicines. It requires a preparation area reserved for this purpose. It is forbidden to smoke, eat or drink in this area.
Personnel must be provided with appropriate handling materials, notably long sleeved gowns, protection masks, caps, protective goggles, sterile single-use gloves, protective covers for the work area and collection bags for waste.
Syringes and infusion sets should be assembled carefully to avoid leakage (use of Luer lock fittings is recommended).

Spills and leakages must be wiped up, wearing protective gloves.

Precautions should be taken to avoid exposing staff during pregnancy.
All contact with eyes must be strictly avoided. Immediate washing of the eye with normal saline solution should be undertaken if any contact occurs. In case of irritation contact an ophthalmologist.

In case of skin contact, thoroughly wash the affected area with water.

On completion, any exposed surface should be thoroughly cleaned and hands and face washed.

For single use only.

Any unused product or waste material should be disposed of in accordance with local requirements.

<u>Preparation of the solution for infusion.</u>
There is no incompatibility between Vinorelbine and glass vials, PVC bag, vinyl acetate bag or polypropylene syringe.

In case of polychemotherapy, Vinorelbine should not be mixed with other agents.

The intra-thecal route is contraindicated.

Vinorelbine must only be administered by the intravenous rout as an infusion.

Vinorelbine may be administered by slow bolus (6-10 minutes) after dilution in 20-50ml of normal saline or glucose 50mg/ml (5%) solution or by a short infusion (20-30 minutes) after dilution in 125ml of normal saline or glucose 50mg/ml (5%) solution. Administration should always be followed with at least 250 ml of a isotonic solution infusion to flush the vein.

Vinorelbine should only be given intravenously. It is very important to make sure that the cannula is accurately placed in the vein before the injection is commenced. If vinorelbine infiltrates the surrounding tissue during intravenous administration, a substantial irritation may occur. In this case, the injection should be stopped, the vein flushed with saline solution and the rest of the dose should be administered in another vein. In the event of extravasation, glucocorticoids could be given intravenously to reduce the risk of phlebitis.

Excreta and vomit must be handled with care.

Storage
As packaged for sale: Store in a refrigerator (2°C - 8°C). Keep the vial in the outer carton in order to protect from light. Do not use Vinorelbine after the expiry date which is stated on the label and carton after EXP. The expiry date refers to the last day of that month.

After first opening
The contents of the vial should be used immediately after the first opening of vial.

After dilution: Following dilution with physiological sodium chloride solution or 50 mg/mL (5%) glucose solution, the chemical and physical stability of the reconstituted solution has been confirmed for 24 hours at 2 – 8°C and not above 25°C at concentrations from 0.5 mg/ml to 3.0 mg/ml.
From a microbiological point of view the product should be used immediately.
If not used immediately, in-use storage times and conditions are the responsibility of the user and would normally not be longer than 24 hours at 2-8°C, unless dilution has taken place in controlled and validated aseptic conditions.

Disposal
Any unused product or waste material should be disposed of in accordance with local requirements.