SANDOZ

אפריל 2025

רופא/ה נכבד/ה,

רוקח/ת נכבד/ה,

חברת סנדוז פרמצבטיקה ישראל בע"מ מבקשת להודיעכם על עדכון העלון לרופא של התכשיר:

VINORELBIN "EBEWE" 10 MG/ML

Concentrate for solution for infusion

מרכיב פעיל: VINORELBINE (AS TARTRATE) 10mg/ml

ההתוויות המאושרות לתכשיר:

For the treatment of non small cell lung cancer.
For the treatment of advanced breast cancer.
Hormone- refractory prostate cancer, especially in combination with low dose oral corticoid therapy or Estramustin.

אנא ראו מטה את העדכונים.

העלון לרופא נשלח לפרסום במאגר התרופות באתר משרד הבריאות:

https://israeldrugs.health.gov.il/#!/byDrug

כמו כן ניתן לקבלו מודפס על ידי פניה לחברת סנדוז פרמצבטיקה ישראל בע"מ.

לעדכונכם בברכה,

מגר' דפנה סנדובסקי

רוקחת ממונה

סנדוז פרמצבטיקה ישראל בע"מ

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ת.ד. 9015, תל אביב, 6109001, ישראל

עדכון העלון לרופא:

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4.4 Special warnings and precautions for use

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Strictly for intravenous use only.

Close haematological monitoring should be performed during treatment (determination of haemoglobin level and number of leucocytes, neutrophils and platelets before each new infusion), since inhibition of the haematopoietic system is the main risk during treatment with vinorelbine.

The dose has to be determined according to the haematological status.

- Neutropenia, which is non-cumulative and has its nadir between day 7 and 14 after administration, and is quickly reversible within 5-7 days, is the main dose-limiting adverse reaction. If the number of neutrophil granulocytes is below 1500/mm^3 and/or the platelet count is below 100000/mm^3, the treatment should be postponed until recovery.

- If the patient presents signs or symptoms suggestive of infection, a prompt investigation should be carried out.

- Interstitial lung disease has been reported more frequently in the Japanese population. Special attention should be exercised for this specific population.

Special precautions for use

- Special caution is advised in patients with a history of ischaemic heart disease (see section 4.8).
- The pharmacokinetics of vinorelbine is not modified in patients presenting moderate or severe liver impairment. For dosage adjustment in this specific patient group, see section 4.2.
- As there is a low level of renal excretion there is no pharmacokinetic rationale for reducing the dose of vinorelbine in patients with impaired kidney function. See section 4.2.
- Vinorelbin "Ebewe" should not be given concomitantly with radiotherapy if the treatment field includes the liver.
- Vinorelbin "Ebewe" must not get into contact with the eye; there is a risk of severe irritation and even corneal ulceration if the drug is sprayed under pressure. If this occurs, immediately rinse the eye with normal saline solution and contact an ophthalmologist.
- Strong inhibitors or inducers of CYP3A4 can affect the vinorelbine concentration and caution should therefore be exercised (see section 4.5 Interactions specific to vinorelbine), and its combination with phenytoin (like all cytotoxics) and with itraconazole (like all vinca alkaloids) is not recommended.
- This product is generally not recommended in combination with live attenuated vaccines and is specifically contra-indicated with yellow fever vaccine.
- Women of child-bearing potential must use effective contraception during treatment and up to ~~3~~7 months after treatment (see section 4.6). For information on pregnancy, breast feeding and fertility, please refer to section 4.6.

~~Since inhibition of the hematopoietic system is the main risk associated with vinorelbine, treatment should be administered under close haematological monitoring (determination of haemoglobin level and leukocyte, neutrophil and platelet counts on the day of each new administration).~~

~~The dose limiting adverse reaction is mainly neutropenia. This effect is non cumulative, having its nadir between the 7th and the 14th day after the administration and is rapidly reversible within 5 to 7 days following treatment.~~

~~If the neutrophil count is below 1500/mm3 and/or the platelet count is below 100,000/mm3, the treatment should be delayed until recovery of these parameters.~~

~~If patients present signs or symptoms suggestive of infection, a prompt investigation should be carried out.~~

~~Special precautions for use~~

~~Special care should be taken when prescribing for patients with a history of ischaemic heart disease (see section 4.8).~~

~~The pharmacokinetics of vinorelbine is not modified in patients with moderate or severe liver impairment. For dosage adjustment in this specific patient group, see section 4.2.~~

~~Given the minor renal excretion, there is no pharmacokinetic justification for reducing the dose of vinorelbine in patients with renal impairment (see section 4.2).~~

~~Vinorelbine should not be given concomitantly with radiotherapy if the treatment field includes the liver.~~

~~This product is specifically contraindicated with yellow fever vaccine and its concomitant use with other live attenuated vaccines is not recommended.~~

~~Caution must be exercised when combining vinorelbine with strong inhibitors or inducers of cytochrome CYP3A4 (see section 4.5 – Vinorelbine-specific interactions). Furthermore, its concomitant use with phenytoin (as with all cytotoxics) and with itraconazole (as with all vinca alkaloids) is not recommended.~~

~~All contact with the eyes should be strictly avoided: risk of severe irritation and even corneal ulceration if the drug is sprayed under pressure. In case of contact, immediately wash the eye with 9 mg/ml (0.9%) sodium chloride solution for injection.~~

~~Interstitial lung disease has been reported more frequently in the Japanese population. Special attention should be given when dealing with this specific population.~~

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4.5 Interactions with other medicinal products and other forms of interactions

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With concomitant administration of phenytoin there is the risk of exacerbation of convulsions resulting from a decreased phenytoin absorption as well as the risk of decreased efficacy of the cytostatic due to increased hepatic metabolism induced by phenytoin. This combination is not recommended.

~~Phenytoin: Risk of exacerbation of convulsions resulting from the decrease of phenytoin digestive absorption by cytotoxic drug or loss of efficacy of the cytotoxic drug due to increased hepatic metabolism by phenytoin.~~

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Vinorelbine-specific interactions:

The combination of vinorelbine with other drugs with known bone marrow toxicity is likely to exacerbate the myelosuppressive adverse effects.

~~As CYP3A4 is mainly involved in the metabolism of vinorelbine, a combination with strong inhibitors of this isoenzyme (e.g., ketoconazole and itraconazole) could increase blood concentrations of vinorelbine, and a combination with strong inducers of this isoenzyme (e.g. rifampicin, phenytoin) could decrease blood~~

~~concentrations of vinorelbine.~~

~~There is no mutual pharmacokinetic interaction when combining vinorelbine with cisplatin over several cycles of treatment. However, the incidence of granulocytopenia associated with vinorelbine use in combination with cisplatin is higher than associated with vinorelbine single agent.~~

CYP3A4 is the main enzyme involved in the metabolism of vinorelbine, and the combination with a drug that induces (such as phenytoin, phenobarbital, rifampicin, carbamazepine, Hypericum perforatum) or inhibits (such as itraconazole, ketoconazole, HIV protease inhibitors, erythromycin, clarithromycin, telithromycin, nefazodone), this iso-enzyme can decrease or increase the concentration of vinorelbine in the blood.

The combination vinorelbine-cisplatin (a very common combination) shows no interaction with respect to the pharmacological parameters of vinorelbine over several cycles of treatment. However, a higher incidence of granulocytopenia has been reported in patients receiving combination therapy with vinorelbine and cisplatin than in those receiving vinorelbine alone.

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4.6 Fertility, pregnancy and lactation

Pregnancy

~~There are no data on the use of vinorelbine in pregnant women.~~
~~Studies in animals have shown embryotoxicity and teratogenicity (see section 5.3). Based on the results of animal studies and the pharmacological action of the drug, there is a potential risk of malformation for the embryo and foetus.~~
~~Vinorelbine should therefore not be used during pregnancy unless the expected individual benefit clearly outweighs the potential risks. If pregnancy occurs during treatment, the patient should be advised regarding the risks to the unborn child and should be carefully monitored. Genetic counselling should be considered.~~

There are insufficient data from the use of vinorelbine in pregnant women. In animal reproductive studies vinorelbine was embryotoxicand feto-lethal and teratogenic (see section 5.3). On the basis of the results of animal studies and the pharmacological action of the medicinal product, there is a potential risk of embryonic and foetal abnormalities.

During pregnancy this product should not be used, unless the individual awaited benefit clearly outweighs the potential risks.

If pregnancy occurs during treatment the patient should be informed about the risks for the unborn child and be monitored carefully. The possibility of genetic counselling should be also considered.

Women of child-bearing age

~~Women of child-bearing age have to use effective contraception during treatment and up to 3 months after treatment.~~
Women of child-bearing potential must use effective methods of contraception during and up to ~~3~~7 months after treatment with Vinorelbin "Ebewe" and should inform their doctor if they become pregnant.

Breastfeeding

It is unknown whether vinorelbine is excreted in human breast milk. The excretion of vinorelbine in milk has not been studied in animal studies. A risk to the child cannot be excluded. Consequently, breastfeeding must be discontinued before starting treatment with Vinorelbin "Ebewe"~~vinorelbine~~ (see section 4.3).

Fertility

Vinorelbine can have genotoxic effects. Therefore, men being treated with vinorelbine are advised not to father a child during and for minimum of ~~3~~ 4 months following cessation of treatment. Advice on conservation of sperm should be sought prior to treatment because of the possibility of irreversible infertility due to therapy with vinorelbine.

~~Men being treated with vinorelbine are advised not to father a child during and minimally up to three months after treatment.~~
~~Prior to treatment, advice should be sought for conserving sperm due to the risk of irreversible infertility as a consequence of treatment with vinorelbine.~~

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4.8 Adverse reactions

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Immune system disorders

Common: Allergic reactions (skin reactions, respiratory reactions).

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Nervous system disorders

~~Very common: - Neurologic disorders (G3-4: 2.7%) including loss of deep tendon reflexes~~
~~Weakness of the lower extremities has been reported following extended chemotherapy~~
~~Uncommon: - Severe paraesthesia with sensory and motor symptoms is infrequent~~

~~These disorders are generally reversible.~~

~~Not known: - Headache~~
~~- Drowsiness~~
~~- Ataxia~~

Very common: Neurologic disorders (G 3-4: 2.7%) including loss of deep tendon reflexes. Weakness of the lower extremities after treatment with long duration.

Uncommon: Severe paraesthesia with sensory and motor symptoms (G3-4: < 3%). These effects are generally reversible when the treatment is discontinued.

Rare: Effects on the autonomic nervous system causing intestinal paresis and constipation. Seldom this progresses to paralytic ileus (see also "Gastrointestinal disorders")

Very rare: Guillain-Barré syndrome

Not known: Headache, dizziness, ataxia, posterior reversible encephalopathy syndrome

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Hepatobiliary disorders

~~Very common: - Transient elevations of liver function tests (G1-2) without clinical symptoms were reported (SGOT 27.6% and SGPT 29.3%)~~
~~Not known: - Hepatic disorder~~

Very common: Abnormal liver function values (total bilirubin increased, alkaline phosphatase increased, aspartate aminotransferase increased, alanine aminotransferase increased) (G 1-2) without clinical symptoms were reported (bilirubin, alkaline phosphatase, ASAT in 27,6% and ALAT in 29,3%)

Not known: Impaired hepatic function

Skin and subcutaneous tissue disorders

Very common: - Usually mild alopecia may occur (G3-4: 4.1% with vinorelbine in monotherapy)
Rare: - Generalised cutaneous reactions have been reported with vinorelbine
Not known: - Palmar-plantar erythrodysesthesia syndrome, skin hyperpigmentation (serpentine supravenous hyperpigmentation)

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6.6 Special precautions for disposal and other handling

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All contact with the eye must be strictly avoided. If this occurs, immediately rinse the eye with normal saline solution and contact an ophthalmologist.

~~All contact with the eye must be strictly avoided. Immediate washing of the eye with normal saline solution should be undertaken if any contact occurs.~~

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