VINORELBINE HIKMA®

vinorelbine ditartrate

WARNING

- Vinorelbine Hikma (vinorelbine ditartrate) injection should be administrered under the supervision of a physician experienced in the use of cancer chemotherapeutic agents. This product is for intravenous (IV) use only. Intrathecal administration of other vinca alkaloids has resulted in death. Syringes containing this product should be labeled "WARNING - FOR IV USE ONLY. FATAL if given intrathecally."
- Severe granulocytopenia resulting in increased susceptibility to infection may occur. Granulocyte counts should be ≥1,000 cells/mm³ prior to the administration of Vinorelbine Hikma. The dosage should be adjusted according to complete blood counts with differentials obtained on the day of treatment.
- Caution - it is extremely important that the intravenous needle or catheter be properly positioned before Vinorelbine Hikma is injected. administration of Vinorelbine Hikma may result in extravasation causing local tissue necrosis and/or thrombophlebitis (see Dosage and Administration and Precautions)

PHARMACOLOGICAL PROPERTIES

Vinorelbine is a cytostatic antineoplastic of the vinca alkaloid group.
The molecular target of its activity is tubulin/microtubule dynamic equilibrium.
Vinorelbine inhibits the polymerization of tubulin.
It acts preferentially on mitotic microtubules and affects axonal microtubules only at high concentration. The effects on tubulin spiralization are lower than that with vincristine.
Vinorelbine blocks mitosis in phase G2+M and induces cell death at interphase or at the following mitosis.

PHARMACOKINETIC FEATURES

Following intravenous injection, the plasma pharmacokinetic profile of Vinorelbine is triphasic.
The mean half-life of the terminal phase is 40h. Plasma clearance is very high (approximately 0.8 l/h/kg.)
Tissue uptake of Vinorelbine is intense and sustained.
Fecal excretion is preponderant related to a massive biliary elimination.
Plasma protein binding level is relatively high (50 to 80%).

INDICATIONS

- Non-small cell lung cancer.
- Metastatic breast caner.

DOSAGE AND ADMINISTRATION

Strict intravenous route.

- As a single agent, the usual does is 25 to 30 mg/m² administered weekly.
- In polychemotherapy, the dose and frequency of administration are dependant upon protocol regimen.

The injected dose should be diluted in a saline solution (e.g. 125 ml) and infused over a short period (15 to 20 minutes).
Administration must be followed by a vein wash out using isotonic solution.

- In the event of hepatic insufficiency, the dosage must be reduced.
- Renal insufficiency (see Precautions.)

It is extremely important to ensure that the needle is properly inserted into the vein before starting the injection of Vinorelbine.
If Vinorelbine extravasates into surrounding tissues during intravenous administration, it may cause marked irritation. In such circumstances, the injection should be stopped and the remainder of the dose given via another vein.

- If any accidental contact with the eye occurs rinse immediately with water or isotonic solution.

CONTRA-INDICATIONS

- Pregnancy
- Nursing mothers
- Severe hepatic insufficiency

PRECAUTIONS

- Treatment must be under strict hematological supervision (determination of hemoglobin level, leucocyte and granulocyte count before any new injection).
- In the event of granulocytopenia injection should be delayed until normalization and keep the patient under close surveillance.
- In case of hepatic insufficiency the dosage should be reduced.
- Due to the lack of studies concerning renal insufficiency, caution is highly recommended when initiating treatment.
- Avoid any accidental contamination of the eyes: risk of severe irritation or even corneal ulceration if the drug is projected under pressure (see Dosage and Administration).
- Vinorelbine should not be administered concomitantly with radiotherapy where the field includes the liver.

SIDE EFFECTS

Hematological toxicity

- Limiting toxicity is granulocytopenia (see Precautions).
- Anemia: frequent but moderate.

Neurotoxicity

- *Peripheral:*
  Generally limited to abolition of the deep tendinous reflexes. Parasthesiae are uncommon. Weakness in lower limbs may be observed after prolonged treatment.
- *Digestive autonomic nervous system:*
  The main manifestation is paresia leading to constipation. Rare cases of paralytic ileus have been described.

Gastrointestinal tolerance

- Constipation (see Neurotoxicity).
- Nausea, vomiting: the incidence is relatively low.

Bronchopulmonary tolerance

- Vinorelbine may bring on dyspnea and bronchospasm like others vinca-alkaloids.
  These reactions occur usually a few minutes following injection or several hours later.

Also reported:

- Alopecia (progressive and moderate), jaw pain.
- All extravasation of the drug during intravenous injection may produce severe local reactions which may lead to necrosis (see Dosage and Administration).

OVERDOSAGE

The major of overdose is the onset of a sever granulocytopenia with a risk of infection which may threaten the vital prognosis.

STORAGE

Store between 2-8°C, protected from light.
Do not freeze. Keep in the original container.
After opening, the solution itself or in dilution in saline or glucose solution in a hermetically sealed glass bottle or PVC bags for infusion may be kept for 24 hours at room temperature (below 25°C) and at daylight.

PRESENTATIONS

Vials:
VINORELBINE HIKMA 10 mg: Vinorelbine Ditartrate 13.85 mg equivalent to vinorelbine 10 mg/1 ml
VINORELBINE HIKMA 50 mg: Vinorelbine Ditartrate 69.25 mg equivalent to vinorelbine 50 mg/ 5 ml
Excipients: Water for injection

THIS IS A MEDICAMENT

- A medicament is a product which affects your health, and its consumption contrary to instructions is dangerous.
- Follow the doctor's prescription strictly, the method of use and the instructions of the pharmacist who sold the medicament.
- The doctor and the pharmacist are experts in medicine, its benefits and risks.
- Do not by yourself interrupt the period of treatment prescribed for you.
- Do not repeat the same prescription without consulting your doctor.

Manufactured by:
Thymoorgan Pharmazie GmbH, Germany
For:
Hikma Pharmaceuticals, Amman - Jordan

Keep medicament out of the reach of children

2INVNRB-E-01/2009