VCR™

Vincristine Sulfate USP IV Injection

DESCRIPTION

VCR™ injection is a preparation of Vincristine Sulfate. Vincristine Sulfate has been related to the inhibition of microtubule formation in mitotic spindle, resulting in an arrest of dividing cells at the metaphase stage. This inhibition has been linked to a reversible binding of the drug to microtubule and spindle proteins in S phase. Vincristine has also been associated with an interference of RNA synthesis. Whether as a result or independent of these actions, Vincristine has been shown to arrest cells in metaphase. Current principles of cancer chemotherapy involve the simultaneous use of several agents. Generally, each agent used has a unique toxicity and mechanism of action so that therapeutic enhancement occurs without additive toxicity. It is rarely possible to achieve equally good results with single–agent methods of treatment. Thus, Vincristine Sulfate is often chosen as part of polychemotherapy because of lack of significant bone–marrow suppression (at recommended doses) and of unique clinical toxicity (neuropathy).

INDICATIONS

VCR™ injection is indicated for the treatment of acute leukemia.

It has also been shown to be useful in combination with other oncolytic agents in Hodgkin's disease, soft-tissue sarcoma, bony-tissue sarcoma, sarcomas of specialized structures, breast cancer, small cell cancer of the lung, cancer of the uterine cervix, malignant melanoma, colorectal cancer, non-Hodgkin's lymphoma, and Wilms' tumor.

DOSAGE AND ADMINISTRATION

VCR™ injection is for intravenous use only at weekly intervals.

The usual dose of **VCR™** injection for pediatric patients is 1.5–2 mg/m^2. For pediatric patients weighing 10 kg or less, the starting dose should be 0.05 mg/kg, administered once a week.

The usual dose of **VCR™** injection for adults is 1.4 mg/m^2. A 50% reduction in the dose of **VCR™** injection is recommended for patients having a direct serum bilirubin value above 3 mg/100 mL.

This preparation is for intravenous use only. It should be administered by individuals experienced in the administration of Vincristine Sulfate injection. The intrathecal administration of Vincristine Sulfate injection usually results in death.

TO REDUCE THE POTENTIAL FOR FATAL MEDICATION ERRORS DUE TO INCORRECT ROUTE OF ADMINISTRATION, VINCRISTINE SULFATE INJECTION SHOULD BE DILUTED IN A FLEXIBLE PLASTIC CONTAINER.

The diluted solution should be infused via a flexible plastic container either directly into a vein or into the tubing of a running intravenous infusion. Infusion of the solution may be completed over approximately 5 to 10 minutes.

THE INJECTION SHOULD BE PROMINENTLY LABELED –

"FOR INTRAVENOUS USE ONLY – FATAL IF GIVEN BY OTHER ROUTES."

CONTRAINDICATIONS

Patients with the demyelinating form of Charcot-Marie-Tooth Syndrome should not be given Vincristine Sulfate Injection.

SIDE EFFECTS

In general, adverse reactions are reversible and are related to dosage. The most common adverse reaction is hair loss; the most troublesome adverse reactions are neuromuscular in origin.

When single, weekly doses of the drug are employed, the adverse reactions of leukopenia, neuritic pain, and constipation occur but are usually of short duration (i.e., less than 7 days). When the dosage is reduced, these reactions may lessen or disappear. The severity of such reactions seems to increase when the calculated amount of drug is given in divided doses. Other adverse reactions, such as hair loss, sensory loss, paresthesia, difficulty in walking, slapping gait, loss of deep–tendon reflexes, and muscle wasting, may persist for at least as long as therapy is continued. Generalized sensorimotor dysfunction may become progressively more severe with continued treatment. Although most such symptoms usually disappear by about the sixth week after discontinuance of treatment, some neuromuscular difficulties may persist for prolonged periods in some patients. Regrowth of hair may occur while maintenance therapy continues.

PRECAUTIONS AND WARNINGS

- Acute uric acid nephropathy, which may occur after the administration of oncolytic agents, has also been reported with Vincristine Sulfate. In the presence of leukopenia or a complicating infection, administration of the next dose of Vincristine Sulfate injection warrants careful consideration.
- If central nervous system leukemia is diagnosed, additional agents may be required, because Vincristine does not appear to cross the blood–brain barrier in adequate amounts. Particular attention should be given to dosage and neurologic side effects if Vincristine Sulfate injection is administered to patients with preexisting neuromuscular disease and when other drugs with neurotoxic potential are also being used.
- Acute shortness of breath and severe bronchospasm have been reported following the administration of vinca alkaloids. These reactions have been encountered most frequently when the vinca alkaloid was used in combination with mitomycin–C and may require aggressive treatment, particularly when there is preexisting pulmonary dysfunction. The onset of these reactions may occur minutes to several hours after the vinca alkaloid is injected and may occur up to 2 weeks following the dose of mitomycin. Progressive dyspnea requiring chronic therapy may occur. Vincristine Sulfate should not be re-administered.
- Care must be taken to avoid contamination of the eye with concentration of Vincristine Sulfate injection used clinically. If accidental contamination occurs severe irritation (or, if the drug was delivered under pressure, even corneal ulceration) may result. The eye should be washed immediately and thoroughly.
- Following administration of Vincristine Sulfate injection, some individuals may have a fall in the white blood cell count or platelet count, particularly when previous therapy or the disease itself has reduced bone–marrow function. Therefore, a complete blood count should be done before administration of each dose. Acute elevation of serum uric acid may also occur during induction of remission in acute leukemia; thus, such levels should be determined frequently during the first 3 to 4 weeks of treatment or appropriate measures taken to prevent uric acid nephropathy.

USE IN PREGNANCY AND LACTATION

Vincristine Sulfate can cause fetal harm when administered to a pregnant woman. There are no adequate and well-controlled studies in pregnant women. If this drug is used during pregnancy or if the patient becomes pregnant while receiving this drug, she should be apprised of the potential hazard to the fetus. Women of childbearing potential should be advised to avoid becoming pregnant. It is not known whether this drug is excreted in human milk. Because many drugs are excreted in human milk and because of the potential for serious adverse reactions due to Vincristine Sulfate in nursing infants, a decision should be made either to discontinue nursing or the drug, taking into account the importance of the drug to the mother.

DRUG INTERACTION

The simultaneous oral or intravenous administration of phenytoin alongside antineoplastic chemotherapy that includes Vincristine Sulfate has been reported to lower blood levels of the anticonvulsant and increase the risk of seizure activity. Therefore, dosage adjustments should be based on regular monitoring of blood levels. This interaction may occur due to reduced absorption of phenytoin and an increased rate of its metabolism and elimination.

Caution should be exercised in patients who are taking medications known to inhibit drug metabolism through hepatic cytochrome P450 isoenzymes in the CYP3A subfamily or in those with liver dysfunction. Additionally, the concurrent administration of Vincristine Sulfate with Itraconazole, a known inhibitor of this metabolic pathway, has been reported to lead to an earlier onset and/or increased severity of neuromuscular side effects. This interaction is believed to be related to the inhibition of vincristine metabolism.

OVERDOSE

Side effects following the use of Vincristine Sulfate injection are dose-related. In pediatric patients under 13 years of age, death has occurred following doses of Vincristine Sulfate that were 10 times those recommended for therapy. Severe symptoms may occur in this patient group following dosages of 3 to 4 mg/m2. Adults can be expected to experience severe symptoms after single doses of 3 mg/m2 or more. Therefore, following administration of doses higher than those recommended, patients can be expected to experience exaggerated side effects.

If someone overdoses, provide supportive care that includes the following:

- Prevention of side effects resulting from the syndrome of inappropriate antidiuretic hormone secretion (preventive treatment would include restriction of fluid intake and perhaps the administration of a diuretic affecting the function of Henle's loop and the distal tubule)
- Administration of anticonvulsants
- Use of enemas or cathartics to prevent ileus (in some instances, decompression of the gastrointestinal tract may be necessary)
- Monitoring the cardiovascular system
- Determining daily blood counts for guidance in transfusion requirements

PHARMACEUTICAL PRECAUTION

Store in a refrigerator (2 °C to 8 °C temperature). Keep away from light & wet place. Keep out of reach of children.

The diluted solution should be used immediately. If not used immediately, in-use storage times and conditions prior to use are the responsibility of the user and should not be longer than 6 hours at room temperature (15 °C to 25 °C) or 24 hours if refrigerated (2 °C to 8 °C), that is, only if the dilution has taken place in controlled and validated aseptic conditions.

PACKAGING

VCR™ IV Injection: Each box contains 2 mg Vincristine Sulfate USP in 2 mL solution.

SK+F ONCOLOGY
Manufactured by
ESKAYEF PHARMACEUTICALS LTD.
RUPGANJ, NARAYANGANJ, BANGLADESH
TM TRADEMARK
R/PM2403 V01