# Vinstin

## Vincristine Sulfate USP

**Composition:**
**Vinstin :** Each vial contains 2 ml solution containing Vincristine Sulfate USP 2 mg.
**Description:**
Vincristine Sulfate is the salt of an alkaloid obtained from the periwinkle plant (Vinca rasea Linn). Vincristine sulfate is a white or slightly yellow, hygroscopic, amorphous or crystalline powder and is freely soluble in water and slightly soluble in alcohol.
**Pharmacokinetics:**
Pharmacokinetic studies in patients with cancer have shown a triphasic serum decay pattern following rapid intravenous injection. The initial. middle, and terminal half-lives are 5 minutes, 2.3 hours and 85 hours respectively; however the range of the terminal half-life in humans is from 19 to 155 hours. The liver is the major excretory organ in humans and animals; about 80% of an injected dose of vincristine sulfate appears in the faeces and 10% to 20% can be found in the urine. Within 15 to 30 minutes after injection, over 90% of the drug is distributed from the blood into tissue, where it remains tightly, but not irreversibly, bound.
**Indications:**
Vincristine sulfate is indicated in acute leukemia. Vincristine sulfate has also been shown to be useful in combination with other oncolytic agents in Hodgkin's disease, non-Hodgkin's malignant lymphomas (lymphocytic, mixed-cell, histiocytic, undifferentiated, nodular, and diffuse types), rhabdomyosarcoma, neuroblastoma, and Wilms'tumor.
**Dosage and Administration:**
Extreme care must be used in calculating and administering the dose of vincristine, since overdosage may have a very serious or fatal outcome. The drug is given i.v. at weekly intervals. Fatal if given intrathecally. **Adults:** The usual dose of vincristine is 1.4 mg/$m_2$. **Children:** The usual dose of vincristine is 1.5- 2 mg/$m_2$. For children weighing 10 kg or less, the initial dose of vincristine should be 0.05 mg/kg once a week, with careful increasing of dosing thereafter based on effects. Vincristine should not be administered to patients receiving radiation therapy through ports that include the liver. When vincristine is used in combination with L-asparaginase, it should be given 12 to 24 hours prior to administration of the enzyme in order to minimize toxicity because L-asparaginase may reduce hepatic clearance of vincristine. Or, as directed by the registered physician.
**Administration:** Vincristine solution may be injected either directly into a vein or into the tubing of an i.g. infusion. Injection of the solution may be completed in about 1 minute. **Further dilution:** The solution may be further diluted with 0.9% sodium chloride injection or 0.5% dextrose injection if desired.
**Contraindication:**
Patients with the demyelinating form of Charcot-Marie-Tooth Syndrome should not be given vincristine sulfate. Vincristine should not be administered to patients while they are receiving radiation therapy through ports that include the liver. Patients with known hypersensitivity to vinca alkaloids or mannitol should not be given vincristine sulfate.
**Precautions:**It is extremely important to be certain that the needle is properly positioned in the vein before any vincristine is injected. If leakage into the surrounding tissue should occur during i.v. administration of vincristine, it may cause considerable irritation. The injection should be discontinued immediately, and any remaining portion of the dose should then be introduced into another vein. Local injection of hyaluronidase and the application of moderate heat to the area of leakage help disperse the drug and are thought to minimize discomfort and the possibility of cellulitis. Vincristine should be used only by physicians experienced in cytotoxic chemotherapy.The drug is very irritating and should not be given intramuscularly, subcutaneously or intrathecally. Intrathecal administration of vincristine is usually fatal. Treatment of patients following accidental intrathecal administration of vincristine has included immediate removal of spinal fluid and flushing with Lactated Ringer's solution, as well as other solutions and has not prevented ascending paralysis and death. In one case, progressive paralysis in an adult was arrested by the following treatment initiated immediately after the intrathecal injection: Vincristine is a vesicant and may cause a severe local reaction on extravasation. If leakage into the surrounding tissue should occur during intravenous administration of vincristine, the injection should be discontinued immediately and any remaining portion of the dose should be introduced into another vein. Local injection of hyaluronidase with the application of heat has been used to disperse the drug in order to minimise discomfort and the possibility of tissue damage. Leucopenia is less likely following therapy with vincristine than is the case with other oncolytic agents. The risk/benefit should be considered in patients with a history of gout or urate renal stones, as acute uric acid nephropathy, which may occur after the administration of oncolytic agents, has also been reported with vincristine. As vincristine penetrates the blood-brain barrier poorly, additional agents and routes of administration may be required for central nervous system leukaemia. The neurotoxic effect of vincristine may be additive with other neurotoxic agents or increased by spinal cord irradiation and neurological disease. Particular attention should be given to dosage and neurologic side effects if vincristine is administered to patients who have had previous cytotoxic drug therapy or irradiation and in those with pre-existing neuromuscular disease (including sensory peripheral neuropathy and steroid-induced myopathy), and also when other drugs with neurotoxic potential are 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 and may require aggressive treatment, particularly when there is pre-existing pulmonary dysfunction. Vincristine should not be readministered.
**Overdose:**
Overdosage with vincristine produces adverse reactions that are mainly extensions of the common adverse effects as these are dose related. As no antidote for vincristine has been found to date, treatment is purely supportive and symptomaticIn children under 13 years of age, death has occurred following doses of vincristine that were ten times those recommended for therapy. Severe symptoms may occur in this patient group following dosages of 3 to 4 . Adults can be expected to experience severe symptoms after single doses of 3 mg/$m_2$ or more. Anticonvulsants such as phenobarbitone may be beneficial in controlling seizures. If profound neutropenia develops, surveillance for the presence of infection by culture, protective isolation and early treatment with antibiotics when infection is suspected, may be necessary. Fluid restriction and possibly the use of an appropriate diuretic may have to be instituted to prevent side effects resulting from hypersecretion of antidiuretic hormone. Enemas may be used to
**Adverse reaction:**
Prior to the use of this drug, patients and or parents/guardians should be advised of the possibility of untoward symptoms. 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. The following adverse reactions have been reported: **Hypersensitivity:** Rare cases of allergic-type reactions, such as anaphylaxis, rash, and oedema, that are temporarily related to vincristine therapy have been reported in patients receiving vincristine as a part of multidrug chemotherapy regimens. **Gastrointestinal:** Autonomic toxicity such as constipation and paralytic ileus are not uncommon and are frequently associated with abdominal cramps. Stool softeners, mild laxatives and enemas may be helpful. A routine prophylactic regimen of laxative and enemas is usually recommended for patients receiving vincristine. Constipation may take the form of upper colon impaction, and on physical examination, the rectum may be empty. Colicky abdominal pain coupled with an empty rectum may mislead the physician. **Genitourinary Hyperuricaemia:** It may occur in some patients receiving vincristine, especially those with non-Hodgkin's lymphomas or leukaemia. In some patients uric acid nephropathy may result. These effects may be minimised by adequate hydration, alkalinisation of the urine and/or administration of allopurinol. Polyuria, dysuria, and urinary retention due to bladder atony have occurred. **Cardiovascular:** Hypertension and hypotension have occurred. Chemotherapy combinations that have included vincristine sulfate, when given to patients previously treated with mediastinal radiation, have been associated with coronary artery disease and myocardial infarction. Causality has not been established. **Neurologic:** Frequently, there is a sequence to the development of neuromuscular side effects. Initially, only sensory impairment and paraesthesiae may be encountered. With continued treatment, neuritic pain and later, motor difficulties may occur. There have been no reports made of any agent that can reverse the neuromuscular manifestations that may accompany therapy with vincristine. **Other:** Fever and headache have occurred. Also other side effects include defective sweating, myoclonic jerks, abnormal Vasalva response, impotence and diminished libido. Weight loss has been reported at high doses.
**Pregnancy and Lactation:** Category D. There are no adequate and well controlled studies in pregnant woman Vincristine has been reported to be found in human milk. Patient recieves Vincristine should not be breast feed.
**Drug Interactions:**
Allopurinol may increase the incidence of cytotoxic induced bone-marrow depression. The mechanism for this potentiation has not been fully classified. The neurotoxicity of vincristine may be additive with that of asparaginase isoniazid and other drugs acting on the peripheral nervous system. The concurrent use of doxorubicin with vincristine and prednisone may produce increased myelosuppression; it is recommended that the combination be avoided. Vincristine appears to increase the cellular uptake of methotrexate by malignant cells and this principle has been applied in high-dose methotrexate therapy.
**Storage:**
Store in a refrigerator at $2_0$ C - $8_0$ C. Do not freeze. Protect from light. Keep out of the reach of children.
**Packaging:**
**Vinstin :** Each box contains 1 vial of 2 ml.

**DRUG INTERNATIONAL LTD.**
**UNIT-2**
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