

Respiratory effects: 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.

Genitourinary effects: Polyuria, dysuria, and urinary retention due to bladder atony have occurred. Other drugs known to cause urinary retention (particularly in the elderly) should, if possible, be discontinued for the first few days following administration of vincristine sulphate.

Neurological effects: Frequently, there is sequence to the development of neuromuscular side effects. Initially, only sensory impairment and paresthesia 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 sulphate. Loss of deep tendon reflexes, foot drop, ataxia, and paralysis have been reported with continued administration. Cranial nerve manifestations, including isolated paresis and paralysis of muscles controlled by cranial motor nerves, may occur in absence of motor impairment elsewhere, extraocular and laryngeal muscles are those most commonly involved. Jaw pain, pharyngeal pain, parotid gland pain, bone pain, back pain, limb pain, and myalgias have been reported, pain in these areas may be severe. Convulsions, frequently with hypertension, have been reported in a few patients receiving Vincristine sulphate. Several instances of convulsions followed by coma have been reported in paediatric patients.

Cutaneous effects:

Alopecia, hyperhidrosis, and dermatic exfoliation have been reported.

Ocular effects:

Transient cortical blindness and optic atrophy with blindness have been reported.

Hypersensitivity:

Rare cases of allergic type reactions, such as anaphylaxis, rash, and edema, that are temporally related to Vincristine sulphate therapy have been reported in patients receiving Vincristine sulphate as a part of multidrug chemotherapy regimens.

Others: Fever, headache, dyslogia, and weight reduction have occurred.

USE IN PREGNANCY AND NURSING MOTHERS

Vincristine sulphate can cause fetal harm when administered to a pregnant woman. When pregnant mice and hamster were given doses of Vincristine sulphate that caused the resorption of 23% to 85% of fetuses, fetal malformations were produced in those that survived.

Five monkeys were given single doses of Vincristine sulphate between days 27 and 34 of their pregnancies, 3 of the fetuses were normal at term, and 2 viable fetuses had grossly evident malformations at term.

In several animal species, Vincristine sulphate can induce teratogenesis as well as embryo death that is nontoxic to the pregnant animal. There are no adequate and well-controlled studies in pregnant woman. If this drug is used during pregnancy or if the patients become pregnant while receiving this drug, she should be apprised of the potential hazard to the fetus. Woman 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 sulphate 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.

CLINICAL TEST EFFECTS

Because dose limiting clinical toxicity is manifested as neurotoxicity, clinical evaluation (eg, history, physical examination) is necessary to detect the need for dosage modification. Following administration of Vincristine sulphate, 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. The laboratory performing these tests should be consulted for its range of normal values.

OVERDOSAGE

Side effect following the use of Vincristine sulphate are dose related. Extreme care must be used in calculating and administering the dose of Vincristine sulphate since overdosage may have a very serious or fatal outcome. Do not exceed 2 mg total once dose. Therefore, following administration of doses higher than those recommended, patients can be expected to experience exaggerated side effects.

Supportive care should include:

Prevention of side-effects resulting from the syndrome of inappropriate antidiuretic hormone. This includes 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; and Determining daily blood counts for guidance in transfusion requirements. Folinic acid has been observed to have a protective effect in normal mice that were administered lethal doses of vincristine sulphate. Isolated case reports suggest that folinic acid may be helpful in treating humans who have received an overdose. It is suggested that 100 mg of folinic acid be administered intravenously every 3 hours for 24 hours and then every 6 hours for at least 48 hours. Theoretically (based on pharmacokinetic data), tissue levels of vincristine sulphate can be expected to remain significantly elevated for at least 72

hours. Treatment with folinic acid does not eliminate the need for the above-mentioned supportive measures.

Side effects following the use of CRISVIN Injection are dose related. In children under 13 years of age, death has occurred following doses of vincristine sulphate 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.

CONTRAINDICATIONS

Patients with the demyelinating form of Charcot-Marie-Tooth syndrome.

Patients with moderate hypersensitivity to the drug.

Vincristine sulphate should be administered with caution in following patients.

Patients with hepatic impairment.

Patients with renal dysfunction.

Patients with bone marrow suppression.

Patients with complicating infection.

Patients who had history of neuromuscular disease. Patients with chickenpox

(Fetal systemic disorder could occur.)

DRUG INTERACTIONS

The simultaneous oral or intravenous administration of phenytoin and antineoplastic chemotherapy combinations that included vincristine sulphate has been repeated to reduce blood levels of the anticonvulsant and to increase seizure activity. Dosage adjustment should be based on serial blood level monitoring. The contribution of vincristine sulphate to this interaction is not certain. The interaction may result from reduced absorption of phenytoin and an increase in the rate of its metabolism and elimination.

STORAGE & INSTRUCTIONS

Store between 2-8°C.

Protect from sunlight, heat & moisture. Keep in a refrigerator, avoid freezing. Keep out of the reach of children.

To be sold on the prescription of a registered oncologist or on demand from cancer hospitals and institutions only.

HOW SUPPLIED

Crisvin 1mg/1ml

1 vial

Crisvin 2mg/2ml

1 vial

خوراک و طریقہ استعمال:

سرطان کے ڈاکٹر کی ہدایت کے مطابق استعمال کریں۔

ہدایات:

دوا کو ۲-۸ ڈگری سینٹی گریڈ درجہ حرارت کے درمیان رکھیں۔

دھوپ، گرمی اور نمی سے محفوظ رکھیں۔

بچوں کی پہنچ سے دور رکھیں۔

صرف مسترد اکولو جسٹ یا کینسر ہسپتال کے نسخہ پر فروخت کریں۔

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