MITONCO for Inj.

Mitomycin 10 mg

COMPOSITION
Each vial contains
Mitomycin ····· 10 mg (potency)
Excipients : D-mannitol, Water for Injection

DESCRIPTION
Blue-purple, freeze-dried crystalline cake in an amber vial

INDICATIONS
Mitomycin is successfully used to improve subjective and objective symptoms in a wide range of neoplastic conditions including chronic lymphatic leukemia, chronic myelocytic leukemia, gastric cancer, colonic and rectal cancer, pulmonary cancer, pancreatic cancer, hepatocarcinoma, uterocervical cancer, mastocarcinoma, tumor of the head and neck, bladder tumor.

PHARMACODYNAMICS
Mitomycin is an antitumour antibiotic that is activated in the tissues to an alkylating agent which disrupts deoxyribonucleic acid (DNA) in cancer cells by forming a complex with DNA and also acts by inhibiting division of cancer cells by interfering with the biosynthesis of DNA.

PHARMACOKINETICS
In vivo, Mitomycin is rapidly cleared from the serum after intravenous administration. The time required to reduce the serum concentration by 50% after a 30mg bolus injection is 17 minutes. After injection of 30 mg, 20 mg or 10 mg intravenously, the maximal serum concentrations were 2.4 mcg/mL, 1.7 mcg/mL and 0.52 mcg/mL respectively. Clearance is effected primarily by metabolism in the liver, but metabolism occurs in other tissues as well. The rate of clearance is inversely proportional to the maximal serum concentration because, it is thought, of saturation of the degradative pathways. Approximately 10% of a dose of Mitomycin is excreted unchanged in the urine. Since metabolic pathways are saturated at relatively low doses, the percentage dose excreted in the urine increases with increasing dose. In children, the excretion of intravenously administered Mitomycin is similar to that in adults.

DOSAGE & ADMINISTRATION
1) Intermittent administration
Usually for adults, 4 to 6mg (potency)/day of Mitomycin is administered intravenously once or twice a week.

2) Administration on consecutive days
Usually for adults, 2mg (potency)/day of Mitomycin is administered intravenously every day.

3) Intermittent massive administration
Usually for adults, 10 to 30mg (potency)/day of Mitomycin is administered intravenously every one to 3 weeks or at longer intervals.

4) Concurrent use with other antineoplastic agents
Usually for adults, 2 to 4mg (potency)/day of Mitomycin is administered once or twice a week in combination with other antineoplastic agents.

Mitonco may be administered, if necessary, intraarterially, intramedullarily, intrapleurally or intraperitoneally at a usual dose of 2 to 10mg (potency)/day of mitomycin in adults. The dosage may be adjusted depending on the age and symptoms of the patient.

5) Use in patients with bladder tumor
For prophylactic use against recurrence, 4 to 10mg (potency) of Mitomycin is usually administered intravesically once every day or every other day.

For therapeutic use, 10 to 40mg (potency)/day of mitomycin is administered intravesically once a day. The dosage may be adjusted depending on the age and symptoms of the patient.

WARNINGS
Bone marrow suppression, notably thrombocytopenia and leukopenia, which may contribute to overwhelming infections in an already compromised patient, is the most common and severe of the toxic effects of mitomycin.
Hemolytic uremic syndrome (HUS) has been reported by use of the drug.

CONTRAINDICATIONS
Patients who have demonstrated a hypersensitive or idiosyncratic reaction to it in the past
Patients who have a history of idiosyncrasy
Patients with thrombocytopenia, coagulation disorder, or an increase in bleeding tendency due to other causes
Patients who are pregnant and are breast-feeding
Patients who are administered yellow fever vaccine or phenytoin as a prophylactic drug

CAUTIONS
Patients with hepatic failure
Patients with renal impairment
Patients with bone marrow suppression
Patients with infection as a complication
Patients with chickenpox

ADVERSE REACTIONS
Gastrointestinal : Anorexia, nausea, vomiting, stomatitis, gastritis, and diarrhea may occur.
Cardiac : Congestive heart failure has rarely been reported.
Respiratory : Pneumonitis, pulmonary fibrosis may occur. If the symptom occurs, it should be discontinued.
Hematologic : Thrombocytopenia, leukopenia, hemorrhagia, anemia, and Hemolytic uremic syndrome may occur. Patients should be monitored regularly.
Urologic : In the case of instillation into the bladder, necrotic cystitis, urethrostenosis may occur.
Hepatic : Rarely, hepatic failure may occur.
Renal : Renal failure may occur as a component of a hemolytic uremic syndrome in patients receiving mitomycin. Hypertension, edema, hematuria, albuminuria has occurred in some patients receiving mitomycin. Patients should be monitored regularly.
Hypersensitivity : Rashes are rarely reported.
Extravasation : Necrosis, skin slough and cellulites of the injection site may occur due to extravasation of the drug.
Others : Rarely headache, blurred vision, confusion, edema, drowsiness, syncope, fatigue, hematemesis, and pain may occur.

PRECAUTIONS
Mitomycin should be administered under the supervision of a qualified physician experienced in the use of cancer chemotherapeutic agents. Appropriate management of therapy and complications is possible only when adequate diagnostic and treatment facilities are readily available.
In case of contact of the drug with the eye, wash the eye thoroughly with water. If the substance is splashed accidentally onto the skin, wash the skin with large amounts of water. Rinse thoroughly.
Patients receiving Mitomycin should be informed of the drug's potential toxicity, particularly bone marrow suppression; death secondary to Mitomycin -induced leukopenia and subsequent has been reported. Patients should be monitored regularly.
Infectious and hemorrhagic complication could occur, therefore should be cautioned.
Use in children or patients aged who are possible to be parents should be considered of the effect on gonad.
Patients receiving Mitomycin should be observed for evidence of renal toxicity. Mitomycin should not be given to patients with a serum creatinine greater than 1.7 mg%.
In case of tumor treatment, the danger of thrombotic crisis could be increased, therefore it should be administered anticoagulant frequently.

DRUG INTERACTIONS
Concomitant of combination with other malignant antitumor agent or irradiation, bone marrow suppression could be occur, therefore state of patients should be monitored regularly and be cautioned with the reduction of dose.
Acute shortness of breath and severe bronchospasm have been reported following the administration of vinca alkaloids (i.e. vincristine sulfate, vinblastine sulfate and vindesine sulfate) in patients who had previously or simultaneously received mitomycin.
In case of combination with phenytoin, hepatic metabolism of cytotoxic substance may increase concomitant to use of busulfan, ifosfamide, etoposide and teniposide.
Combination with yellow fever vaccine could cause generalized or fetal disease, therefore combination with the drug should be avoided.
In case of combination with doxorubicin, cardiotoxicity may increase because of formation of free radical.
Possibility of lung damage has been reported due to uratic nitrogen, and doxorubicin.
Barbiturate may increase the effect of the drug.

USE IN PREGNANCY AND NURSING MOTHERS
Mitomycin has produced teratogenic effects in animals. Safe use of Mitomycin in pregnant women has not been established.
Safe use of Mitomycin in lactation has not been established. Therefore, administration of mitomycin should be discontinued when receiving Mitomycin therapy.

USE IN PEDIATRIC
Safety of Mitomycin in pediatric patients has not been established. Administration should be cautioned to appearance of adverse effects.

USE IN THE ELDERLY
Administration in the elderly should be cautioned to dose and the interval of dose according to patient's state.

OVERDOSAGE
Fever, nausea, vomiting, and bone marrow suppression may occur. If it occurs, appropriate therapy should be administered.

PHARMACEUTICAL PRECAUTIONS
Cellulitis at the injection site has occurred and is occasionally severe.
Care should be taken to avoid extravation of the drug. It is extremely important that the needle be properly positioned in the vein before this product is injected. If leakage into surrounding tissue should occur during intravenous administration of Mitomycin, it may cause sclerosis and necrosis.
Care must be taken to avoid contamination of the eye with concentrations of Mitomycin used clinically. If accidental contamination occurs, the eye should be washed with 8.4% sodium hydrogen carbonate ophthalmic solution immediately and thoroughly.

INSTRUCTION FOR USE
Mitomycin powder for injection is reconstituted by adding 5 mL of sterile water for injection to a vial labeled as containing 2 mg of mitomycin, to provide a solution containing approximately 0.4 mg/mL. The vial should be shaken to enhance dissolution; if the powder for injection does not dissolve immediately, allow the vial to stand at room temperature until complete dissolution occurs.

STORAGE
Preserve in hermetic containers, protected from light.
Store at room temperature not exceeding 30°C.

PACKAGE
1 Vial/Box

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