Adverse Reactions

Bone Marrow Toxicity: This was the most common and most serious toxicity, occurring in 60% of 937 patients (64.4%). Thrombocytopenia and/or leukopenia may occur anytime within 6 weeks after onset of therapy with an average time of 4 weeks. Recovery after cessation of therapy was within 10 weeks. About 25% of the leukopenic or thrombocytopenic episodes did not recover. Mitomycin produces cumulative myelosuppression.

Integument and Mucous Membrane Toxicity: This has occurred in approxi- mately 10% of patients treated with MUTAMYCIN (mitomycin for injection, USP). Cellulitis at the injection site has been reported and is occasionally severe. Stomatitis and alopecia also occur frequently. Rashes are rarely reported but are of no importance within this dose range. Other non-hematologic side effects that may occur include the iritis, the necrosis and consequent sloughing of tissue which results if the drug is extravasated during extravasation. Extravasation may occur with or without an accompanying stinging or burning sensation and even if there is adequate blood return when the needle injection is aspirated. There have been reports of delayed edema and/or ulceration occurring either at or distal to the injection site. weeks to months after MUTAMYCIN, even when no obvious evidence of extravasation was observed during administration. Skin grafting has been required in some of the cases.

Renal Toxicity: 2% of 1,281 patients demonstrated a significantly reduced renal function. The creatinine clearance at doses indicated.

MUTAMYCIN® (mitomycin for injection, USP) (also known as mitomycin (mitomycin for injection, USP)

The use of MUTAMYCIN results in a high incidence of bone marrow sup- pression, particularly thrombocytopenia and leukopenia. Therefore, the fol- lowing studies should be obtained repeatedly during therapy and for at least eight weeks following therapy: platelet count, white blood cell count, differential, and hemoglobin. The occurrence of a platelet count below 100,000/mm3 or a WBC below 4,000/mm3 or a progressive decline in either is an indication to with- draw further therapy until blood counts have recovered above these levels.

Patients should be advised of the potential toxicity of this drug, particularly bone marrow suppression. Deaths have been reported due to sepsisemia as a result of leukopenia due to the drug.

Patients receiving MUTAMYCIN should be observed for evidence of renal toxicity. MUTAMYCIN should not be given to patients with a serum creatinine greater than 1.7 mg percent.

Usage in Pregnancy: Safe use of MUTAMYCIN in pregnant women has not been established. Teratological changes have been noted in animal stud- ies. The effect of MUTAMYCIN on fertility is unknown.

PRECAUTIONS

Acute shortness of breath and severe bronchospasm have been reported fol- lowing the administration of vinca alkaloids in patients who had previously or simultaneously received MUTAMYCIN. The onset of this acute respiratory dis- tress occurred within minutes to hours after the vinca alkaloid injection. The total number of doses for each drug has varied considerably. Bronchodilators, steroids, and/or oxygen have produced symptomatic relief.

A few cases of adult respiratory distress syndrome have been reported in patients receiving MUTAMYCIN in combination with other chemotherapeutic agents and as palliative treatment when other modalities may have been due to the primary or metastatic disease processes. Malaise and anesthesia have been reported as part of postmarketing surveillance. Bladder fibrosis/contraction has been reported with intravesical admin- istration (not an approved route of administration), which in rare cases has resulted in cystectomy.