Dacarzin

Dacarbazine Injection

COMPOSITION

Dacarzin Injection: Each vial contains Dacarbazine BP 200 mg as sterile lyophilized powder.

CLINICAL PHARMACOLOGY

Dacarbazine acts by inhibiting cell replication. Since Dacarbazine is an analogue of 5-amino-imidazole-4-carboxamide, It might interfere with purine biosynthesis and hence DNA bio-synthesis. One metabolite of Dacarbazine, diazomethane, is an alkylating agent and act in the same way of Nitrogen mustards. The drug might act as a sulphydryl reagent since the inhibition of bacterial growth by Dacarbazine.

PHARMACODYNAMICS

The antineoplastic effect of Dacarbazine is due to an inhibition of cell growth. An alkylating effect has also been shown and other cytostatic mechanisms may also be influenced by Dacarbazine. Dacarbazine is considered not to show an antineoplastic effect by itself. However by Microsomal N-demethylation it is quickly converted to 5-amino-imidaz-ole-4-carboxamide and a methyl cation, which is responsible for the alkylating effect of the medicinal product.

PHARMACOKINETICS

Absorption

The drug is recommended for intravenous administration only. Peak plasma concentration of about 8 micrograms per ml is reached immediately following administration of Dacarbazine.

Distribution

After intravenous administration Dacarbazine is quickly distributed into tissue. Plasma protein binding is 5 %. The initial half-life is only 20 minutes; terminal half-life is 0.5 – 3.5 hours.

Metabolism

Dacarbazine is inactive until metabolized in the liver by cytochromes P450 to form the reactive N-demethylated species HMMTIC and MTIC. This is catalyzed by CYP1A1, CYP1A2, and CYP2E1. MTIC is further metabolized to 5-aminoimidazole-4-carboxamide.

Elimination

Dacarbazine is metabolized mainly in the liver by both hydroxylation and demethylation, approximate 20 – 50 % of the medicinal product is excreted unmodified by the kidney via renal tubular secretion.

INDICATIONS

Advanced Hodgkin's disease

Dacarbazine is indicated for the treatment of advanced Hodgkin's disease with the association of Bleomycin, Doxorubicin and Vinblastine.

Metastatic Malignant Melanoma

Dacarbazine is indicated for the treatment of Metastatic malignant melanoma who has been previously treated with others Nitrogen mustards.

Advanced adult soft tissue sarcomas

Dacarbazine is indicated for the treatment of patients with advanced adult soft tissue sarcomas & others fibro sarcomas.

DOSAGE & ADMINISTRATION

Hodgkin's disease

Dacarbazine is administered in a daily dose of 375 mg/m^2 body surface area intravenously every 15 days in combination with Doxorubicin, Bleomycin and Vinblastine (ABVD regimen).

Malignant melanoma

Dacarbazine can be administered as single agent in doses of 200 to 250 mg/m^2 body surface area/day as an intravenous injection for 5 days every 3 weeks.

Adult soft tissue sarcoma

For adult soft tissue sarcomas Dacarbazine is given in daily doses of 250 mg/m^2 body surface area intravenous (days 1 - 5) in combination with Doxorubicin every 3 weeks (ADIC regimen).

MODE OF ADMINISTRATION

Administration is only by the intravenous route. Reconstitute vial contents by adding 19.7 ml of Water to vial. The resulting solution is hypotonic and will contain Dacarbazine with a pH of 3 to 4.

DOSAGE MODIFICATION

Pediatric

No special information submitted to indicate whether or not children require a different dosage range or whether they metabolize the drug differently or react differently to the drug.

Geriatric

As for pediatric use

With impaired hepatic function

As the drug partly undergoes metabolism in the liver, impairment of liver function is likely to necessitate a variation in dosage.

With impaired renal function

As the drug is excreted 50% unchanged in the urine by tubular secretion, impairment of renal function is likely to necessitate a variation in dosage.

ADVERSE EFFECTS

Hematopoietic depression: Hematopoietic depression is the most serious form of toxicity and involves primarily the leucocytes and megakaryocytes causing depression of platelets. Leucopenia and thrombocytopenia may be severe enough to cause death. Careful monitoring of red and white blood cells and platelets is required.

Bone marrow toxicity: Long-term therapy can cause cumulative bone marrow toxicity.

Immunosuppression: Dacarbazine is a moderate immunosuppressive agent. Administration of live vaccines to patients who are immune compromised can cause serious and potentially fatal infections.

Pulmonary toxicity: Concomitant use of fotemustine can cause acute pulmonary toxicity which may lead to a fatal outcome. Fotemustine and Dacarbazine should not be used concomitantly.

DRUG INTERACTIONS

Microsomal liver enzyme inducers such as barbiturates, rifampicin, and phenytoin may theoretically hasten the activation of Dacarbazine. The incidence or severity of side effects may be altered when Dacarbazine is used in combination with other antineoplastic agents. Additive bone marrow depression may occur if Dacarbazine is administered with other bone-marrow depressants or with radiation therapy. It has been reported that Dacarbazine reduced the response to levodopa in a patient with Parkinson's disease.

CONTRAINDICATIONS

Dacarbazine is contradicted in patients who have severe liver or kidney diseases, leukopenia and thrombocytopenia.

SPECIAL WARNING & PRECAUTIONS

It is recommended that Dacarbazine should only be administered under the supervision of a physician specialized in oncology who has the facilities for regular monitoring of clinical, biochemical and hematological effects, during and after therapy.

OVERDOSAGE

The primary complications of overdose are severe bone marrow suppression, eventually bone marrow aplasia. There is no known antidote for Dacarbazine overdose. Therefore, special care has to be taken to avoid overdose of this medicinal product.

STORAGE CONDITION

Store the vial in original carton in refrigerator at 2°C to 8°C (36°F to 46°F) temperature. Protect from light. Keep out of the reach of children. Retain the vial in the original carton until time of use.

PRESENTATION & PACKAGING

Dacarzin Injection: Each commercial box contains 1 vial of Dacarbazine 200 mg powder for injection.

Manufactured by-
BEACON®
Pharmaceuticals Limited
Bhaluka, Mymensingh, Bangladesh

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