SIZE: 90X260MM

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For the use only of a Registered Medical Practitioner or a Hospital or a Laboratory

Dacarbazine Injection IP 100mg / 200 mg / 500 mg

Deca

Rx only

COMPOSITION

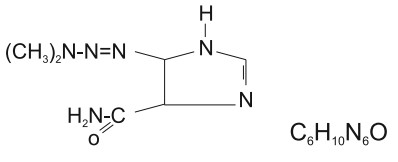
Dacarbazine Injection IP 100 mg
Each vial contains:
Dacarbazine IP 100 mg
Excipients qs

Dacarbazine Injection IP 200 mg
Each vial contains:
Dacarbazine IP 200 mg
Excipients qs

Dacarbazine Injection IP 500 mg
Each vial contains:
Dacarbazine IP 500 mg
Excipients qs

DESCRIPTION

Dacarbazine Injection IP 100 mg & 200 mg is a pale yellow to yellow lyophilized cake or discontinuous powder of free flowing powder in 10 ml, 20 ml vial. Dacarbazine is anticancer agent. Chemically, Dacarbazine for Injection is 5-(3,3-dimethyl-1-triazeno) imidazole-4-carboxamide with molecule formula of $C_6H_{10}N_6O$ and a molecular weight o 182.19. The Structural formula is as follows:



$C_6H_{10}N_6O$

CLINICAL PHARMACOLOGY

After intravenous administration of Dacarbazine the volume of distribution exceeds total body water content suggesting localization in some body tissue, probably the liver. Its disappearance from the plasma is biphasic with initial half-life of 19 minutes and a terminal half- life of 5 hours. In a patient with renal and hepatic dysfunctions, the half-lives were lengthened to 55 minutes and 7.2 hours. The average cumulative excretion of unchanged Dacarbazine in the urine is 40% of the Injected dose in 6 hours. Dacarbazine is subject to renal tubular secretion rather than glomerular filtration. At therapeutic concentrations Dacarbazine is not appreciably bound to human plasma protein.

In man, Dacarbazine is extensively degraded. Besides unchanged Dacarbazine, 5-aminoimidazole-4 carboxamide (AIC) is a major metabolite of Dacarbazine excreted in the urine. AIC is not derived endogenously but from the injected Dacarbazine, because the administration of radioactive Dacarbazine labeled with ^{14}C in the imidazole portion of the molecule (Dacarbazine - 2- ^{14}C) gives rise to AIC -2-C14C.

Although the exact mechanism of action of Dacarbazine is not known, three hypotheses have been offered:

- Inhibition of DNA synthesis by acting as a purine analog.
- Action as an alkylating agent.
- Interaction with SH groups.

INDICATIONS:

Dacarbazine Injection IP 100mg / 200 mg & 500 mg is indicated in the treatment of metastatic malignant melanoma. In addition, Dacarbazine Injection IP 100 mg / 200 mg & 500 mg is also indicated for Hodgkin's disease as a secondary - line - therapy when used in combination with other effective agents.

CONTRAINDICATIONS

Dacarbazine Injection IP 100 mg / 200 mg & 500 mg is contraindicated in patients who have demonstrated a hypersensitivity to it in the past.

WARNINGS:

It is recommended that Dacarbazine Injection IP 100 mg / 200 mg & 500 mg be administered under the supervision of a qualified physician experienced in the use of cancer chemotherapeutic agents.

Studies have demonstrated this agent to have a carcinogenic and teratogenic effect when used in animals. In treatment of each patient, the physician must weigh carefully the possibility of achieving therapeutic benefit against the risk of toxicity.

Hemopoietic depression is the most common toxicity with Dacarbazine and Involves primarily the leukocytes and platelets, although, anemia may sometimes occur. Leukopenia and thrombocytopenia may be severe enough to cause death. The possible bone marrow depression requires careful monitoring of white blood cells, red blood cells, and platelet levels. Hemopioetic toxicity may warrant temporary suspension or cessation of therapy with Dacarbazine.

Hepatic toxicity accompanied by hepatic vein thrombosis and hepatocellular necrosis resulting in death, has been reported. The incidence of such reactions has been low; approximately 0.01% of patients treated. This toxicity has been observed mostly when Dacarbazine has been administered concomitantly with other anti-neoplastic drugs; however, it has also been reported in some patients treated with Dacarbazine alone.

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Anaphylaxis can occur following the administration of Dacarbazine

PRECAUTIONS

Hopitalization is not always necessary but adequate laboratory study capability must be available. Extravasation of the drug subcutaneously during intravenous administration may result in tissue damage and severe pain. Local Pain, burning sensation, and Irritation at the site of Injection may be relieved by locally applied hot packs.

Carcinogenicity of Dacarbazine was studied in rats and mice. Proliferative endocardial lesions, including fibrosarcomas and sarcomas were induced by Dacarbazine in rats. In mice, administration of Dacarbazine resulted in the induction of anglosarcomas of the spleen.

Pregnancy Category C. Dacarbazine has been shown to be teratogenic in rats when given in doses 20 human daily dose to male rats (twice weekly for 9 weeks) did not affect the male libido, although female rats mates to male rats had higher incidence of resorptions than controls. In rabbits, Dacarbazine daily dose 7 times the human daily dose given on Days 6-15 of gestation resulted in fetal skeletal anomalies. There are no adequate and well controlled studies in pregnant women. Dascarbazine should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus.

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 tumorigenicity shown for Dacarbazine in animal studies, a decision should be made whether to discontinue nursing or to discontinue the drug, taking into account the importance of the drug to the mother

ADVERSE REACTIONS

Symptoms of anorexia, nausea, and vomiting are the most frequently noted of all toxic reactions. Over 90% of patients are affected with the initial few doses. The vomiting lasts 1-12 hours and is incompletely and unpredictably palliated with phenobarbital and / or prochlorperazine. Rarely, intractable nausea and vomiting have necessitated discontinuance of therapy with Dacarbazine. Rarely, Dacarbazine has caused diarrhea. Some helpful suggestions include restricting the patient's oral intake of food for 4-6 hours prior to treatment. The rapid toleration of these symptoms suggests that a central nervous system mechanism may be involved, and usually these symptoms subside after the first 1 or 2 days.

There are a number of minor toxicities that are infrequently noted. Patients have experienced an influenza-like syndrome of fever to 39°C, myalgias and malaise. These symptoms occurs usually after large single doses, may last for several days, and they may occur with successive treatments.

Alopecia has been noted as has facial flushing and facial paresthesia. There have been few reports of significant liver or renal function test abnormalities in man. However, these abnormalities have been observed more frerquently in animal studies.

Erythematous and urticarial rashes have been observed infrequently after administration of Dacarbazine. Rarely, photosensitivity reactions may occur.

DOSAGE AND ADMINISTRATION

Malignant Melanoma : The recommended dosage is 2 tp 4.5 mg / kg / day for 10 days. Treatment may be repeated at 4 week intervals.

An alternate recommended dosage is 250mg / m2/ day I.V. for 5 days. Treatment may be repeated every 3 weeks.

Hodgkin's Disease: The recommended dosage of Dacarbazine for Injection IP 100 mg / 200 mg & 500 mg in the treatment of Hodgkin's disease is 150mg/m2/day for 5 days, in combination with other effective drugs. Treatment may be repeated every 4 weeks. An alternative recommended dosage is 375 mg / m2 on day 1, in combination with other effective drugs, to be repeated every 15 days.

Dacarbazine Injection IP 100 mg/vial and 200 mg/vial & 500 mg/vial are reconstituted with 10 ml and 19.7 ml,and49.5 ml Sterile Water for Injections USP. The resulting solution contains 10mg / ml of dacarbazine having a pH of 3.0 to 4.0. The calculated dose of the resulting solution is drawn into a syringe and administrated only intravenously.

The reconstitution and prior to use, the solution in the vial may be stored at 4°C for up to 72 hours or at normal room conditions (temperature and light) for up to 8 hours. If the reconstituted solution is further diluted in 5% Dextrose Injection IP or 0.9% Sodium Chloride Injection IP the resulting solution may be stored at 4°C for up to 24 hours or at normal room conditions for up to 8 hours.

Parenteral drug products should be inspected visually for particulate matter and discoloration prior to administration.

Procedures for proper handling and disposal of anticancer drugs should be considered. Several guidelines on this subject have been published. There is no general agreement that all of the procedures recommended in the guidelines are necessary or appropriate.

OVERDOSE

Give supportive treatment and monitor blood cell counts.

STORAGE

Store the vials in the original carton between 2°C and 8°C (36°F to 46°F). Protect from light.

HOW SUPPLIED

Dacarbazine Injection IP 100 mg
Single Vial, Individually packed in a carton.

Dacarbazine Injection IP 200 mg
Single Vial, Individually packed in a carton.

Dacarbazine Injection IP 500 mg
Single Vial, Individually packed in a carton.

SHELF LIFE

24 Months

Manufactured by:
ADLEY FORMULATIONS PVT. LTD.
(Formerly Known as Adley Formulations)
Vill. Kotla, Barotiwala- 174103
Distt.: Solan, Himachal Pradesh

Marketed by:
NEOVA BIOGENE PRIVATE LIMITED.
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