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

DACTINOMYCIN FOR INJECTION USP 500mcg (0.5 mg)

Dactinomycin™

Rx only **500 mcg (0.5mg)** TAJ PHARMA

COMPOSITION

Dactinomycin 500 mcg (0.5 mg)

Dactinomycin for Injection USP 500 mcg (0.5 mg)

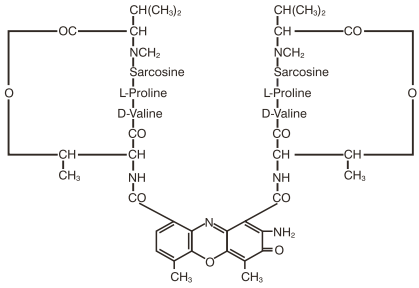
Each sterile lyophilized vial contains

Dactinomycin USP	500 mcg (0.5 mg)
Mannitol USP	20 mg

DESCRIPTION

Dactinomycin is one of the actinomycins, a group of antibiotics produced by various species of Streptomyces. Dactinomycin is the principal component of the mixture of actinomycins produced by Streptomyces parvullus.

The empirical formula is $C_{62}H_{86}N_{12}O_{16}$ and the structural formula is:



Dactinomycin for Injection is a sterile, yellow to orange lyophilized powder for injection by the intravenous route or by regional perfusion after reconstitution. Each vial contains Dactinomycin(0.5 mg) and Mannitol.

CLINICAL PHARMACOLOGY

Mechanism of Action

Generally, the actinomycins exert an inhibitory effect on gram-positive and gram-negative bacteria and on some fungi. However, the toxic properties of the actinomycins (including dactinomycin) in relation to antibacterial activity are such as to preclude their use as antibiotics in the treatment of infectious diseases. This cytotoxic action is the basis for their use in the treatment of certain types of cancer. Dactinomycin is believed to produce its cytotoxic effects by binding DNA and inhibiting RNA synthesis.

Pharmacokinetics

Results of a study in patients with malignant melanoma indicate that dactinomycin (3H actinomycin D) is minimally metabolized, is concentrated in nucleated cells, and does not penetrate the blood-brain barrier. Approximately 30% of the dose was recovered in urine and feces in one week. The terminal plasma half-life for radioactivity was approximately 36 hours.

INDICATIONS AND USAGE

Dactinomycin, as part of a combination chemotherapy and/or multi-modality treatment regimen, is indicated for the treatment of Wilms' tumor, childhood rhabdomyosarcoma, Ewing's sarcoma and metastatic, nonseminomatous testicular cancer.

Dactinomycin is indicated as a single agent, or as part of a combination chemotherapy regimen, for the treatment of gestational trophoblastic neoplasia.

Dactinomycin, as a component of regional perfusion, is indicated for the palliative and/or adjunctive treatment of locally recurrent or locoregional solid malignancies.

CONTRAINDICATIONS

Dactinomycin should not be given at or about the time of infection with chickenpox or herpes zoster because of the risk of severe generalized disease which may result in death.

WARNINGS

Pregnancy Pregnancy Category D

Dactilon may cause fetal harm when administered to a pregnant woman. Dactilon has been shown to cause malformations and embryo toxicity in rat, rabbit, and hamster when given in doses of 50 to 100 mcg/kg (approximately 0.5 - 2 times the maximum recommended daily human dose on a body surface area basis). If this drug is used during pregnancy, or if the patient becomes pregnant while receiving this drug, the patient should be apprised of the potential hazard to the fetus. Women of childbearing potential must be warned to avoid becoming pregnant.

PRECAUTIONS

General

Veno-occlusive disease (primarily hepatic) may result in fatality, particularly in children younger than 48 months.

Carcinogenesis, Mutagenesis, Impairment of Fertility

Dactinomycin has been shown to be mutagenic in a number of test systems ***in vitro*** and **in vivo** including human fibroblasts and leukocytes, and HeLa cells. DNA damage and cytogenetic effects have been demonstrated in the mouse and the rat.

Adequate fertility studies have not been reported, although, reports suggest an increased incidence of infertility following treatment with other antineoplastic agents.

Nursing Mothers

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 in nursing infants from Dactinomycin, a decision should be made as to discontinuation of nursing and/ or drug, taking into account the importance of the drug to the mother.

Pediatric Use

The greater frequency of toxic effects of Dactinomycin in infants suggests that this drug should be administered to infants only over the age of 6 to 12 months.

Geriatric Use

Clinical studies of Dactinomycin did not include sufficient numbers of subjects aged 65 and over to determine whether they respond differently from younger subjects. Other reported clinical experience has not identified differences in responses between the elderly and younger patients.

ADVERSE REACTIONS

Gastrointestinal

Anorexia, nausea, vomiting, abdominal pain, diarrhea, gastrointestinal ulceration. Nausea and vomiting, which occur early during the first few hours after administration, may be alleviated by the administration of anti-emetics.

Hepatic

Liver toxicity including liver function test abnormalities, ascites, hepatomegaly, hepatitis, hepatic failure with reports of death, hepatic veno-occlusive disease which may be associated with intravascular clotting disorder and multi-organ failure.

Hematologic

Anemia, even to the point of aplastic anemia, agranulocytosis, leukopenia, thrombocytopenia, pancytopenia, reticulocytopenia. Platelet and white cell counts should be performed frequently to detect severe hematopoietic depression. If either count markedly decreases, the drug should be withheld to allow marrow recovery. This often takes up to three weeks.

DRUG INTERACTIONS

Drug/Laboratory Test Interactions

Dactinomycin may interfere with bioassay procedures for the determination of antibacterial drug levels.

DOSAGE & ADMINSTRATION

The dosage of Dactinomycin varies depending on the tolerance of the patient, the size and location of the neoplasm, and the use of other forms of therapy. It may be necessary to decrease the usual dosages suggested below when additional chemotherapy or radiation therapy is used concomitantly or has been used previously.

The dosage for Dactinomycin is calculated in micrograms (mcg). The dose intensity per 2-week cycle for adults or children should not exceed 15 mcg/kg/day or 400-600 mcg/ m^2/day intravenously for five days. Calculation of the dosage for obese or edematous patients should be performed on the basis of surface area in an effort to more closely relate dosage to lean body mass.

A wide variety of single agent and combination chemotherapy regimens with Dactinomycin may be employed. Because chemotherapeutic regimens are constantly changing, dosing and administration should be performed under the direct supervision of physicians familiar with current oncologic practices and new advances in therapy. The following suggested regimens are based upon a review of current literature concerning therapy with Dactinomycin and are on a per cycle basis.

Intravenous Use

The dosage for Dactinomycin is calculated in micrograms (mcg). The dose intensity per 2-week cycle for adults or children should not exceed 15 mcg/kg/day or 400-600 mcg/ m²day intravenously for five days. Calculation of the dosage for obese or edematous patients should be performed on the basis of surface area in an effort to more closely relate dosage to lean body mass.

OVERDOSE

Dactinomycin was lethal to mice and rats at intravenous doses of 700 and 500 mcg/kg, respectively (approximately 3.8 and 5.4 times the maximum recommended daily human dose on a body surface area basis, respectively). The oral LD50 of Dactinomycin is 7.8 mg/kg and 7.2 mg/kg in the mouse and rat, respectively.

STORAGE

Store at 25°C (77°F); excursions permitted to 15°C to 30°C (59°F to 86°F). Protect from light.

HOW SUPPLIED

Dactinomycin 500 mcg (0.5 mg)

Dactinomycin for Injection USP 500 mcg (0.5 mg)

Single dose vial, individually packed in a carton.

SHELF LIFE

36 Months

Dactinomycin™

500 mcg (0.5mg)

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™Trade mark owned by Taj Pharmaceuticals Ltd.

Mfg. Lic. No: DD/L/809

Manufactured in India By:

TAJ PHARMACEUTICALS LIMITED

at SURVEY NO.188/1 TO 189/1,190/1 TO 4,
ATHIYAWAD, DABHEL, DAMAN- 396210 (INDIA)

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