WARNING

Dactinomycin for injection should be administered only under the supervision of a physician who is experienced in the use of cancer chemotherapeutic agents.

This drug is HIGHLY TOXIC and both powder and solution must be handled and administered with care. Inhalation of dust or vapors and contact with skin or mucous membranes, especially those of the eyes, must be avoided. Avoid exposure during pregnancy. Due to the toxic properties of dactinomycin (e.g., corrosivity, carcinogenicity, mutagenicity, teratogenicity), special handling procedures should be reviewed prior to handling and followed diligently. Dactinomycin is extremely corrosive to soft tissue. If extravasation occurs during intravenous use, severe damage to soft tissues will occur. In at least one instance, this has led to contracture of the arms.

INDICATIONS AND USAGE

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

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

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. Unlike other species of Streptomyces, this organism yields an essentially pure substance that contains only traces of similar compounds differing in the amino acid content of the peptide side chains. The empirical formula is C_{62}H_{86}N_{12}O_{16} and the structural formula is:
Dactinomycin is a sterile, yellow to orange lyophilized powder for injection by the intravenous route or by regional perfusion after reconstitution. Each vial contains 0.5 mg (500 mcg) of dactinomycin and 20.0 mg of mannitol.

**CLINICAL PHARMACOLOGY**

**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.

Because the actinomycins are cytotoxic, they have an antineoplastic effect which has been demonstrated in experimental animals with various types of tumor implants. 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 and Metabolism:** Results of a study in patients with malignant melanoma indicate that dactinomycin (\(^3\)H 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.

**CLINICAL STUDIES**

A wide variety of single agent and combination chemotherapy regimens with Dactinomycin for injection have been studied. Because chemotherapeutic regimens are constantly changing, the decision to employ Dactinomycin for injection should be directly supervised by physicians familiar with current oncologic practices and new advances in therapy.

**Wilms’ Tumor:** The neoplasm responding most frequently to Dactinomycin for injection is Wilms’ tumor. Data from the National Wilms’ Tumor Studies (NWTS-1, NWTS-2, NWTS-3 and NWTS-4) support the use of Dactinomycin in Wilms’ tumor. The NWTS-3 evaluated results in 1,439 patients randomized to various regimens incorporating Dactinomycin (see table below).

<table>
<thead>
<tr>
<th>The Third National Wilms’ Tumor Study</th>
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<tbody>
<tr>
<td>Stage</td>
</tr>
<tr>
<td>-------</td>
</tr>
<tr>
<td>I (favorable histology)</td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td>II (favorable histology)</td>
</tr>
</tbody>
</table>
L = Dactinomycin and vincristine (10 weeks)
EE = Dactinomycin and vincristine (26 weeks)
DD = Dactinomycin, doxorubicin, and vincristine (65 weeks)
DD1 = Dactinomycin, doxorubicin, and vincristine (65 weeks) preceded by radiation therapy (1000 rads)
DD2 = Dactinomycin, doxorubicin, and vincristine (65 weeks) preceded by radiation therapy (2000 rads)
DD-RT = Dactinomycin, doxorubicin, and vincristine (65 weeks) preceded by radiation therapy (dose according to age)
K = Dactinomycin and vincristine (65 weeks)
K1 = Dactinomycin and vincristine (65 weeks) preceded by radiation therapy (1000 rads)
K2 = Dactinomycin and vincristine (65 weeks) preceded by radiation therapy (2000 rads)
J = Dactinomycin, doxorubicin, cyclophosphamide, and vincristine (65 weeks)

It should be noted that the complete results from NWTS-4 have not yet been published. Changes in NWTS-4 and NWTS-5 have consisted of alterations in duration as well as dose intensity of Dactinomycin. As a consequence, appropriate consultation with physicians experienced in the management of Wilms’ tumor should be sought.

Childhood Rhabdomyosarcoma: The Third Intergroup Rhabdomyosarcoma Study (IRS-III) studied 1,062 previously untreated pediatric patients and young adults (≤21 years of age) and compared outcomes amongst a number of treatment regimens.

Dactinomycin was included in all arms as a standard component of the treatment regimen; thus, comparative data are not available from this study. Nevertheless, it does provide information on treatment outcomes in a large group of closely studied patients. For treatment purposes, patients were stratified according to clinical group, histologic subtype, and site of disease. Patients in most strata were randomized, but clinical group I patients with favorable histology were not randomized and treated according to a single regimen.

<table>
<thead>
<tr>
<th>The Third Intergroup Rhabdomyosarcoma Study</th>
<th>Group</th>
<th>Number of Arms</th>
<th>Chemotherapy Regimen</th>
<th>5-Year Progression Free Survival (%) (mean±SEM)</th>
<th>5-Year Overall Survival (%) (mean±SEM)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>I</td>
<td>1 (non randomized)</td>
<td>cyclic sequential VA (1 year)</td>
<td>83±3</td>
<td>93±2</td>
</tr>
</tbody>
</table>
Metastatic Nonseminomatous Testicular Cancer: Combinations of vinblastine, cyclophosphamide, Dactinomycin, bleomycin and cisplatin (VAB-6 regimen) have been employed in the treatment of metastatic nonseminomatous testicular cancer. In a retrospective analysis of 142 evaluable patients with primary advanced stage II or clinical stage III testicular cancer 112 (79%) achieved a complete response (CR) after treatment with VAB-6 alone or in combination with surgery. Relapses were uncommon (12%) and 117 of 166 patients (71%) were categorized as alive without evidence of disease during the four years covered by the study.

Ewing’s Sarcoma: Dactinomycin in conjunction with vincristine, doxorubicin, cyclophosphamide and radiotherapy has been used in the management of both metastatic and non-metastatic Ewing’s sarcoma. Of 120 previously untreated patients with non-metastatic disease treated with Dactinomycin as part of maintenance therapy in the United Kingdom Children’s Cancer Study Group Ewing’s Tumor Study (ET-1), 49 (41%) were free of disease at 5 years and 53 (44%) were alive at 5 years. Outcomes in regional and metastatic disease for previously untreated patients administered Dactinomycin resulted in 31 of 44 patients (70%) achieving a CR after a median time on study of 83 weeks. Eight of 44 (18%) patients achieved a partial response (PR) and the remaining 5 (11%) demonstrated no response to the regimen.

Gestational Trophoblastic Neoplasia: Single agent Dactinomycin has been used in the management of nonmetastatic gestational trophoblastic neoplasia. In a series of 31 patients with nonmetastatic disease, complete and sustained remissions were achieved with Dactinomycin alone in 94% of treated patients. Alternating combination regimens incorporating Dactinomycin in conjunction with etoposide, methotrexate, vincristine and cyclophosphamide (EMA-CO regimen) have also been used in the treatment of poor prognosis gestational trophoblastic neoplasia. Administration of EMA-CO to 148

<table>
<thead>
<tr>
<th>II (favorable histology, excluding orbit, head and paratesticular sites)</th>
<th>2 (randomized)</th>
<th>VA, doxorubicin and RT (1 year) VA and RT (1 year)</th>
<th>77±6</th>
<th>56±10</th>
<th>89±5</th>
<th>54±13</th>
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</thead>
<tbody>
<tr>
<td>III (excluding special pelvic, orbit, scalp, parotid, oral cavity, larynx, oropharynx and cheek)</td>
<td>3 (randomized)</td>
<td>pulsed VAC and RT (2 years) pulsed VADRC-VAC, CDDP and RT (2 years) pulsed VADRC-VAC, CDDP, VP-16 and RT (2 years)</td>
<td>70±6</td>
<td>62±5</td>
<td>56±4</td>
<td>70±6</td>
</tr>
<tr>
<td>IV (all)</td>
<td>3 (randomized)</td>
<td>pulsed VAC and RT (2 years) pulsed VADRC-VAC, CDDP and RT (2 years) pulsed VADRC-VAC, CDDP, VP-16 and RT (2 years)</td>
<td>27±8</td>
<td>27±8</td>
<td>30±6</td>
<td>27±6</td>
</tr>
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</table>

VA = vincristine/Dactinomycin  
VADRC = vincristine/doxorubicin/cyclophosphamide  
VAC = vincristine/Dactinomycin/cyclophosphamide  
CDDP = Cisplatin  
VP-16 = Etoposide  
RT = radiation therapy
women with poor prognosis gestational trophoblastic neoplasia resulted in 110 (80%) complete and 25 (18%) partial responses after a mean follow-up of 50.4 months. Overall survival during the study period was 85% and relapses were uncommon (5.4%). Meticulous monitoring of beta-hCG (human chorionic gonadotropin) must be incorporated into the treatment regimen.

Regional Perfusion in Locally Recurrent and Locoregional Solid Malignancies: Dactinomycin, as a component of regional perfusion, has been administered as palliative treatment and as an adjunct to tumor resection in the management of locally recurrent and locoregional sarcomas, carcinomas and adenocarcinomas.

CONTRAINDICATIONS
Hypersensitivity to any component of this product.

Dactinomycin for injection 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
Reports indicate an increased incidence of second primary tumors (including leukemia) following treatment with radiation and antineoplastic agents, such as Dactinomycin. Multi-modal therapy creates the need for careful, long-term observation of cancer survivors.

Pregnancy Category D: Dactinomycin may cause fetal harm when administered to a pregnant woman. Dactinomycin has been shown to cause malformations and embryotoxicity in rat, rabbit, and hamster when given in doses of 50-100 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: This drug is HIGHLY TOXIC and both powder and solution must be handled and administered with care (see boxed warning and HOW SUPPLIED, Special Handling). Since Dactinomycin is extremely corrosive to soft tissues, it is intended for intravenous use. Inhalation of dust or vapors and contact with skin or mucous membranes, especially those of the eyes, must be avoided. Appropriate protective equipment should be worn when handling Dactinomycin. Should accidental eye contact occur, copious irrigation for at least 15 minutes with water, normal saline or a balanced salt ophthalmic irrigating solution should be instituted immediately, followed by prompt ophthalmologic consultation. Should accidental skin contact occur, the affected part must be irrigated immediately with copious amounts of water for at least 15 minutes while removing contaminated clothing and shoes. Medical attention should be sought immediately. Contaminated clothing should be destroyed and shoes cleaned thoroughly before reuse (see HOW SUPPLIED, Special Handling).

As with all antineoplastic agents, Dactinomycin is a toxic drug and very careful and frequent observation of the patient for adverse reactions is necessary. These reactions may involve any tissue of the body, most commonly the hematopoietic system resulting in myelosuppression. As such, live virus vaccines should not be administered during therapy with Dactinomycin. The possibility of an anaphylactoid reaction should be borne in mind.

It is extremely important to observe the patient daily for toxic side effects when combination chemotherapy is employed, since a full course of therapy occasionally is not tolerated. If stomatitis, diarrhea, or severe hematopoietic depression appear during therapy, these drugs should be discontinued until the patient has recovered.

Veno-occlusive Disease: Veno-occlusive disease (primarily hepatic) may result in fatality, particularly
in children younger than 48 months. (See ADVERSE REACTIONS, Hepatic.)

**Dactinomycin for Injection and Radiation Therapy:** An increased incidence of gastrointestinal toxicity and marrow suppression has been reported with combined therapy incorporating Dactinomycin for injection and radiation. Moreover, the normal skin, as well as the buccal and pharyngeal mucosa, may show early erythema. A smaller than usual radiation dose administered in combination with Dactinomycin causes erythema and vesiculation, which progress more rapidly through the stages of tanning and desquamation. Healing may occur in four to six weeks rather than two to three months. Erythema from previous radiation therapy may be reactivated by Dactinomycin alone, even when radiotherapy was administered many months earlier, and especially when the interval between the two forms of therapy is brief. This potentiation of radiation effect represents a special problem when the radiotherapy involves the mucous membrane. When irradiation is directed toward the nasopharynx, the combination may produce severe oropharyngeal mucositis. Severe reactions may ensue if high doses of both Dactinomycin and radiation therapy are used or if the patient is particularly sensitive to such combined therapy.

Particular caution is necessary when administering Dactinomycin for injection within two months of irradiation for the treatment of right-sided Wilms’ tumor, since hepatomegaly and elevated AST levels have been noted. In general, Dactinomycin should not be concomitantly administered with radiotherapy in the treatment of Wilms’ tumor unless the benefit outweighs the risk.

**Dactinomycin for Injection and Regional Perfusion Therapy:** Complications of the perfusion technique are related mainly to the amount of drug that escapes into the systemic circulation and may consist of hematopoietic depression, absorption of toxic products from massive destruction of neoplastic tissue, increased susceptibility to infection, impaired wound healing, and superficial ulceration of the gastric mucosa. Other side effects may include edema of the extremity involved, damage to soft tissues of the perfused area, and (potentially) venous thrombosis.

**Laboratory Tests:** Many abnormalities of renal, hepatic, and bone marrow function have been reported in patients with neoplastic diseases receiving Dactinomycin. Renal, hepatic, and bone marrow functions should be assessed frequently.

**Drug/Laboratory Test Interactions:** Dactinomycin may interfere with bioassay procedures for the determination of antibacterial drug levels.

**Carcinogenesis, Mutagenesis, Impairment of Fertility:** Reports indicate an increased incidence of second primary tumors (including leukemia) following treatment with radiation and antineoplastic agents, such as Dactinomycin. Multi-modal therapy creates the need for careful, long-term observation of cancer survivors.

The International Agency on Research on Cancer has judged that dactinomycin is a positive carcinogen in animals. Local sarcomas were produced in mice and rats after repeated subcutaneous or intraperitoneal injection. Mesenchymal tumors occurred in male F344 rats given intraperitoneal injections of 50 mcg/kg, 2 to 5 times per week for 18 weeks. The first tumor appeared at 23 weeks.

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.

**Pregnancy:** Pregnancy Category D

(See WARNINGS.)

**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 suggest 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. However, a published meta-analysis of all studies performed by the Eastern Cooperative Oncology Group (ECOG) over a 13-year period suggests that administration of Dactinomycin to elderly patients may be associated with an increased risk of myelosuppression compared to younger patients. In general, dose selection for an elderly patient should be cautious, usually starting at the low end of the dosing range, reflecting the greater frequency of decreased hepatic, renal, or cardiac function, and of concomitant disease or other drug therapy.

**ADVERSE REACTIONS**

Toxic effects (excepting nausea and vomiting) usually do not become apparent until two to four days after a course of therapy is stopped, and may not peak until one to two weeks have elapsed. Deaths have been reported. However, adverse reactions are usually reversible on discontinuance of therapy. They include the following:

- **Miscellaneous:** Sepsis (including neutropenic sepsis) with fatal outcome, infection, malaise, fatigue, lethargy, fever, myalgia, proctitis, hypocalcemia and growth retardation.
- **Oral:** Cheilitis, dysphagia, esophagitis, ulcerative stomatitis, pharyngitis.
- **Lung:** Pneumonitis.
- **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 (see PRECAUTIONS, Veno-occlusive Disease).
- **Hematologic:** Anemia, even to the point of aplastic anemia, agranulocytosis, leukopenia, thrombocytopenia, pancytopenia, reticulocytopenia, neutropenia, febrile neutropenia. 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.
- **Dermatologic:** Alopecia, skin eruptions, acne, erythema multiforme, flare-up of erythema or increased pigmentation of previously irradiated skin. Toxic Epidermal Necrolysis (TEN) and Stevens Johnson Syndrome (SJS) have been observed from postmarketing experience.
- **Soft tissues:** Dactinomycin is extremely corrosive. If extravasation occurs during intravenous use, severe damage to soft tissues will occur. In at least one instance, this has led to contracture of the arms. Epidermolysis, erythema, and edema, at times severe, have been reported with regional limb perfusion.
- **Laboratory Tests:** Many abnormalities of renal, hepatic, and bone marrow function have been reported in patients with neoplastic diseases receiving Dactinomycin. Renal, hepatic, and bone marrow functions should be assessed frequently.

To report SUSPECTED ADVERSE REACTIONS, contact Prasco Laboratories, at 1-866-525-0688 or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

**OVERDOSAGE**
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.

Manifestations of overdose in patients have included nausea, vomiting, diarrhea, mucositis including stomatitis, gastrointestinal ulceration, severe skin disorders including skin exfoliation, exanthema, desquamation and epidermolysis, severe hematopoietic depression, veno-occlusive disease, acute renal failure, sepsis (including neutropenic sepsis) with fatal outcome and death. No specific information is available on the treatment of overdosage with Dactinomycin. Treatment is symptomatic and supportive. It is advisable to check skin and mucous membrane integrity as well as renal, hepatic, and bone marrow functions frequently.

**DOSAGE AND ADMINISTRATION**

**Not for oral administration:** Toxic reactions due to Dactinomycin are frequent and may be severe (see ADVERSE REACTIONS), thus limiting in many instances the amount that may be administered. However, the severity of toxicity varies markedly and is only partly dependent on the dose employed.

Careful calculation of the dosage should be performed prior to administration of each dose.

**Intravenous Use:** 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 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/m2/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.

**Wilms’ Tumor, Childhood Rhabdomyosarcoma and Ewing’s Sarcoma:** Regimens of 15 mcg/kg intravenously daily for five days administered in various combinations and schedules with other chemotherapeutic agents have been utilized in the treatment of Wilms’ tumor, rhabdomyosarcoma and Ewing’s sarcoma.

**Metastatic Nonseminomatous Testicular Cancer:** 1000 mcg/m2 intravenously on Day 1 as part of a combination regimen with cyclophosphamide, bleomycin, vinblastine, and cisplatin.

**Gestational Trophoblastic Neoplasia:** 12 mcg/kg intravenously daily for five days as a single agent. 500 mcg intravenously on Days 1 and 2 as part of a combination regimen with etoposide, methotrexate, folinic acid, vincristine, cyclophosphamide and cisplatin.

**Regional Perfusion in Locally Recurrent and Locoregional Solid Malignancies:** The dosage schedules and the technique itself vary from one investigator to another; the published literature, therefore, should be consulted for details. In general, the following doses are suggested:

- 50 mcg (0.05 mg) per kilogram of body weight for lower extremity or pelvis.
- 35 mcg (0.035 mg) per kilogram of body weight for upper extremity.

It may be advisable to use lower doses in obese patients, or when previous chemotherapy or radiation therapy has been employed.
Preparation of Solution for Intravenous Administration: This drug is HIGHLY TOXIC and both powder and solution must be handled and administered with care (see boxed warning and HOW SUPPLIED, Special Handling). Since Dactinomycin is extremely corrosive to soft tissues, it is intended for intravenous use. Inhalation of dust or vapors and contact with skin or mucous membranes, especially those of the eyes, must be avoided. Appropriate protective equipment should be worn when handling Dactinomycin. Should accidental eye contact occur, copious irrigation for at least 15 minutes with water, normal saline or a balanced salt ophthalmic irrigating solution should be instituted immediately, followed by prompt ophthalmologic consultation. Should accidental skin contact occur, the affected part must be irrigated immediately with copious amounts of water for at least 15 minutes while removing contaminated clothing and shoes. Medical attention should be sought immediately. Contaminated clothing should be destroyed and shoes cleaned thoroughly before reuse. (See HOW SUPPLIED, Special Handling.)

Reconstitute Dactinomycin by adding 1.1 mL of Sterile Water for Injection (without preservative) using aseptic precautions. The resulting solution of Dactinomycin will contain approximately 500 mcg (0.5 mg) per mL.

Parenteral drug products should be inspected visually for particulate matter and discoloration prior to administration, whenever solution and container permit. When reconstituted, Dactinomycin is a clear, gold-colored solution.

Once reconstituted, the solution of Dactinomycin can be added to infusion solutions of Dextrose Injection 5 percent or Sodium Chloride Injection either directly or to the tubing of a running intravenous infusion.

Although reconstituted Dactinomycin is chemically stable, the product does not contain a preservative and accidental microbial contamination might result. Any unused portion should be discarded. Use of water containing preservatives (benzyl alcohol or parabens) to reconstitute Dactinomycin for Injection, results in the formation of a precipitate.

Studies conducted on dactinomycin lyophilized powder for injection demonstrate that drug product diluted at concentrations of 10 mcg/mL or higher in WFI, 0.9% saline and 5% dextrose in glass or PVC infusion containers are chemically stable for up to 10 hours when stored at ambient room temperature. Drug product diluted to concentrations lower than 10 mcg/mL and stored at ambient room temperature showed significantly lower recoveries. Therefore, only drug product diluted at concentrations greater than 10 mcg/mL are recommended for administration. Since the product contains no preservatives, the final prepared product (which has undergone reconstitution and dilution) must be used within 4 hours of initial reconstitution when stored at ambient room temperature.

Partial removal of Dactinomycin from intravenous solutions by cellulose ester membrane filters used in some intravenous in-line filters has been reported.

Since dactinomycin is extremely corrosive to soft tissue, precautions for materials of this nature should be observed.

If the drug is given directly into the vein without the use of an infusion, the “two-needle technique” should be used. Reconstitute and withdraw the calculated dose from the vial with one sterile needle. Use another sterile needle for direct injection into the vein. Discard any unused portion of the Dactinomycin solution.

Management of Extravasation: Care in the administration of Dactinomycin will reduce the chance of perivenous infiltration (see boxed warning and ADVERSE REACTIONS). It may also decrease the chance of local reactions such as urticaria and erythematous streaking. On intravenous administration of Dactinomycin, extravasation may occur with or without an accompanying burning or stinging sensation, even if blood returns well on aspiration of the infusion needle. If any signs or symptoms of extravasation have occurred, the injection or infusion should be immediately terminated and restarted in another vein. If extravasation is suspected, intermittent application of ice to the site for 15 minutes 4
times daily for 3 days may be useful. The benefit of local administration of drugs has not been clearly
established. Because of the progressive nature of extravasation reactions, close observation and plastic
surgery consultation is recommended. Blistering, ulceration and/or persistent pain are indications for
wide excision surgery, followed by split-thickness skin grafting.

**HOW SUPPLIED**

Dactinomycin for Injection is a lyophilized powder. In the dry form the compound is an amorphous
yellow to orange powder. The solution is clear, gold-colored and essentially free from visible
particles. Dactinomycin for Injection is supplied in vials containing 0.5 mg (500 micrograms) of
dactinomycin and 20.0 mg of mannitol.

NDC 66993-489-83 Single Dose Vial

NDC 66993-489-35 12 Single Dose Vials

**Storage:** Store at 20-25ºC (68-77ºF). See USP controlled room temperature. Protect from light and
humidity.

**Special Handling:** Animal studies have shown dactinomycin to be corrosive to skin, irritating to the
eyes and mucous membranes of the respiratory tract and highly toxic by the oral route. It has also been
shown to be carcinogenic, mutagenic, embryotoxic and teratogenic. Due to the drug’s toxic properties,
appropriate precautions including the use of appropriate safety equipment are recommended for the
preparation of Dactinomycin for parenteral administration. Inhalation of dust or vapors and contact with
skin or mucous membranes, especially those of the eyes, must be avoided. Avoid exposure during
pregnancy. The National Institutes of Health presently recommends that the preparation of injectable
antineoplastic drugs should be performed in a Class II laminar flow biological safety cabinet. Personnel
preparing drugs of this class should wear chemical resistant, impervious gloves, safety goggles, outer
garments and shoe covers. Additional body garments should be used based upon the task being
performed (e.g., sleevelets, apron, gauntlets, disposable suits) to avoid exposed skin surfaces and
inhalation of vapors and dust. Appropriate techniques should be used to remove potentially contaminated
clothing.

Several other guidelines for proper handling and disposal of antineoplastic drugs have been published
and should be considered. [1]- [4]

**Accidental Contact Measures:** Should accidental eye contact occur, copious irrigation for at least 15
minutes with water, normal saline or a balanced salt ophthalmic irrigating solution should be instituted
immediately, followed by prompt ophthalmologic consultation. Should accidental skin contact occur, the
affected part must be irrigated immediately with copious amounts of water for at least 15 minutes while
removing contaminated clothing and shoes. Medical attention should be sought immediately.
Contaminated clothing should be destroyed and shoes cleaned thoroughly before reuse (see
PRECAUTIONS, General and DOSAGE AND ADMINISTRATION, Preparation of Solution for
Intravenous Administration).

**REFERENCES**

1. Preventing Occupational Exposures to Antineoplastic and Other Hazardous Drugs in Health Care
Settings. NIOSH Alert 2004-165.

2. OSHA Technical Manual, TED 1-0.15A, Section VI: Chapter 2. Controlling Occupational Exposure


4. Polovich M, White JM, Kelleher LO (eds.) 2005. Chemotherapy and Biotherapy Guidelines and
Recommendations for Practice. (2nd ed) Pittsburgh, PA: Oncology Nursing Society.
PRINCIPAL DISPLAY PANEL
NDC 66993-489-83
Single Dose Vial
Rx Only
PRASCO
Dactinomycin for Injection
500 mcg (0.5 mg)
For Preparation of Intravenous Solutions
Dactinomycin for Injection
500 mcg (0.5 mg)

For Preparation of Intravenous Solutions

Store at 20-25ºC (68-77ºF).
See USP controlled room temperature. Protect from light and humidity.

DANGER:
Contact Poison. Avoid contact with skin, mucous membranes, or eyes.
Do not inhale the dust or vapor. Incase of contact, wash with copious amounts of water for at least 15 minutes.
See PRECAUTIONS and HOW SUPPLIED in accompanying package insert.

Each Vial contains:
Dactinomycin .................. 500 mcg
Inactive ingredient:
Mannitol ......................... 30 mg

Rx Only
PRASCO

Manufactured by: Baxter Oncology GmbH

NDC 66993-489-35
12 Single Dose Vials
Rx Only
PRASCO
Dactinomycin for Injection
500 mcg (0.5 mg)
Store at 20-25ºC (68-77ºF).
See USP controlled room temperature.
Protect from light and humidity.
Manufactured by: Baxter Oncology GmbH
# DACTINOMYCYN

dactinomycin injection, powder, lyophilized, for solution

## Product Information

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## Active Ingredient/Active Moiety

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<th>Ingredient Name</th>
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<th>Strength</th>
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<tr>
<td>DACTINOMYCYN (UNII: 1CC1JFE158) (DACTINOMYCYN - UNII:1CC1JFE158)</td>
<td>DACTINOMYCYN</td>
<td>0.5 mg in 1 mL</td>
</tr>
</tbody>
</table>

## Inactive Ingredients

<table>
<thead>
<tr>
<th>Ingredient Name</th>
<th>Strength</th>
</tr>
</thead>
<tbody>
<tr>
<td>MANNITOL (UNII: 3OWL53L36A)</td>
<td></td>
</tr>
</tbody>
</table>

## Packaging

<table>
<thead>
<tr>
<th>#</th>
<th>Item Code</th>
<th>Package Description</th>
<th>Marketing Start Date</th>
<th>Marketing End Date</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>NDC:66993-489-35</td>
<td>12 in 1 CARTON</td>
<td>12/04/2017</td>
<td></td>
</tr>
<tr>
<td>NDC:66993-489-83</td>
<td>1 in 1 CARTON</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>------------------</td>
<td>---------------</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1 mL in 1 VIAL, SINGLE-DOSE; Type 0: Not a Combination Product</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

### Marketing Information

<table>
<thead>
<tr>
<th>Marketing Category</th>
<th>Application Number or Monograph Citation</th>
<th>Marketing Start Date</th>
<th>Marketing End Date</th>
</tr>
</thead>
<tbody>
<tr>
<td>NDA authorized generic</td>
<td>NDA050682</td>
<td>12/04/2017</td>
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</tr>
</tbody>
</table>

### Labeler - Prasco Laboratories (065969375)

### Establishment

<table>
<thead>
<tr>
<th>Name</th>
<th>Address</th>
<th>ID/FEI</th>
<th>Business Operations</th>
</tr>
</thead>
<tbody>
<tr>
<td>Baxter Oncology GmbH</td>
<td></td>
<td>344276063</td>
<td>manufacture(66993-489)</td>
</tr>
</tbody>
</table>

Revised: 12/2017