

**DACTINOMYCIN- dactinomycin injection, powder, lyophilized, for solution**  
**Hisun Pharmaceuticals USA, Inc.**

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**HIGHLIGHTS OF PRESCRIBING INFORMATION**

**These highlights do not include all the information needed to use DACTINOMYCIN FOR INJECTION safely and effectively. See full prescribing information for DACTINOMYCIN FOR INJECTION.**

**DACTINOMYCIN for injection for intravenous use**

**Initial U.S. Approval: 1964**

----- **RECENT MAJOR CHANGES** -----

- Dosage and Administration, Recommended Dosage for Wilms Tumor ( 2.1) 8/2018
- Dosage and Administration, Recommended Dosage for Ewing Sarcoma ( 2.3) 8/2018

----- **INDICATIONS AND USAGE** -----

Dactinomycin for injection is an actinomycin indicated for the treatment of:

- adult and pediatric patients with Wilms tumor, as part of a multi-phase, combination chemotherapy regimen. ( 1.1)
- adult and pediatric patients with rhabdomyosarcoma, as part of a multi-phase, combination chemotherapy regimen. ( 1.2)
- adult and pediatric patients with Ewing sarcoma, as part of a multi-phase, combination chemotherapy regimen. ( 1.3)
- adult and pediatric patients with metastatic, nonseminomatous testicular cancer, as part of a multi-phase, combination chemotherapy regimen. ( 1.4)
- post-menarchal patients with gestational trophoblastic neoplasia, as a single agent or as part of a combination chemotherapy regimen. ( 1.5)
- adult patients with locally recurrent or locoregional solid malignancies, as a component of palliative or adjunctive regional perfusion. ( 1.6)

----- **DOSAGE AND ADMINISTRATION** -----

- Wilms Tumor: The recommended dose is 45 mcg/kg intravenously once every 3 to 6 weeks for up to 26 weeks, as part of a multi-agent combination chemotherapy regimen. ( 2.1)
- Rhabdomyosarcoma: The recommended dose is 15 mcg/kg intravenously once daily for 5 days every 3 to 9 weeks for up to 112 weeks, as part of a multi-agent combination chemotherapy regimen. ( 2.2)
- Ewing Sarcoma: The recommended dose is 1250 mcg/m<sup>2</sup> intravenously once every 3 weeks for 51 weeks, as part of a multi-agent combination chemotherapy regimen. ( 2.3)
- Metastatic Nonseminomatous Testicular Cancer: The recommended dose is 1000 mcg/m<sup>2</sup> intravenously every 3 weeks, as part of cisplatin-based, multi-drug chemotherapy regimen. ( 2.4)
- Gestational Trophoblastic Neoplasia:
  - Non-metastatic and Low-risk Metastatic Disease: The recommended dose is 12 mcg/kg intravenously daily for 5 days, as a single agent. ( 2.5)
  - High-risk Metastatic Disease: The recommended dose is 500 mcg intravenously on Days 1 and 2 every 2 weeks for up to 8 weeks, as part of a multi-agent combination chemotherapy regimen. ( 2.5)
- Regional Perfusion in Locally Recurrent and Locoregional Solid Malignancies:
  - Lower Extremity or Pelvis: The recommended dose is 50 mcg/kg once with melphalan. ( 2.6)
  - Upper Extremity: The recommended dose is 35 mcg/kg once with melphalan. ( 2.6)

----- **DOSAGE FORMS AND STRENGTHS** -----

For injection: 500 mcg as a lyophilized powder in a single-dose vial. ( 3)

----- **CONTRAINDICATIONS** -----

None. ( 4)

----- **WARNINGS AND PRECAUTIONS** -----

- Secondary Malignancy or Leukemia: Increased risk of secondary malignancies following treatment. ( 5.1)
- Venous-occlusive Disease: Can cause severe or fatal VOD. Monitor for elevations in AST, ALT, total bilirubin, hepatomegaly, weight gain, or ascites. Consider delaying next dose. ( 5.2)
- Extravasation: Immediately interrupt the injection or infusion and apply ice. ( 2.7, 5.3)

- Myelosuppression: Monitor blood cell counts before each cycle. Delay next dose if severe myelosuppression has not improved. ( 5.4)
- Immunizations: Vaccination with live viral vaccines is not recommended before or during treatment. ( 5.5)
- Severe Mucocutaneous Reactions: Discontinue treatment ( 5.6)
- Renal Toxicity: Monitor creatinine and electrolytes frequently. ( 5.7)
- Hepatotoxicity: Monitor transaminases, alkaline phosphatase and bilirubin prior to and during treatment. ( 5.8)
- Potentiation of Radiation Toxicity and Radiation Recall: Reduce dose by 50% during concomitant radiation. Use caution when administering within two months of radiation. ( 5.9)
- Embryo-fetal Toxicity: Can cause fetal harm. Advise patients of the potential risk to a fetus and to use effective contraception. ( 5.10, 8.1, 8.3)

----- **ADVERSE REACTIONS** -----

Common adverse reactions are: infection, alopecia, rash, dysphagia, fatigue, fever, nausea, vomiting, anemia, neutropenia, thrombocytopenia, mucositis, and hepatotoxicity ( 6)

**To report SUSPECTED ADVERSE REACTIONS, contact Hisun Pharmaceuticals USA, Inc., at 1-855-554-4786 or FDA at 1-800-FDA-1088 or [www.fda.gov/medwatch](http://www.fda.gov/medwatch).**

----- **USE IN SPECIFIC POPULATIONS** -----

Lactation: Advise not to breastfeed. ( 8.2)

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**Revised: 11/2018**

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\* Sections or subsections omitted from the full prescribing information are not listed.

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## **FULL PRESCRIBING INFORMATION**

### **1 INDICATIONS AND USAGE**

#### **1.1 Wilms Tumor**

Dactinomycin for injection is indicated for the treatment of adult and pediatric patients with Wilms tumor, as part of a multi-phase, combination chemotherapy regimen.

#### **1.2 Rhabdomyosarcoma**

Dactinomycin for injection is indicated for the treatment of adult and pediatric patients with rhabdomyosarcoma, as part of a multi-phase, combination chemotherapy regimen.

#### **1.3 Ewing Sarcoma**

Dactinomycin for injection is indicated for the treatment of adult and pediatric patients with Ewing sarcoma, as part of a multi-phase, combination chemotherapy regimen.

#### **1.4 Metastatic Nonseminomatous Testicular Cancer**

Dactinomycin for injection is indicated for the treatment of adult and pediatric patients with metastatic, nonseminomatous testicular cancer, as part of a multi-phase, combination chemotherapy regimen.

#### **1.5 Gestational Trophoblastic Neoplasia**

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

#### **1.6 Regional Perfusion in Locally Recurrent and Locoregional Solid Malignancies**

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

### **2 DOSAGE AND ADMINISTRATION**

## 2.1 Recommended Dosage for Wilms Tumor

The recommended dose of dactinomycin for injection, as part of a multi-agent combination chemotherapy regimen, is 45 mcg/kg intravenously once every 3 to 6 weeks for up to 26 weeks.

## 2.2 Recommended Dosage for Rhabdomyosarcoma

The recommended dose of dactinomycin for injection, as part of a multi-agent combination chemotherapy regimen, is 15 mcg/kg intravenously once daily for 5 days every 3 to 9 weeks for up to 112 weeks.

## 2.3 Recommended Dosage for Ewing Sarcoma

The recommended dose of dactinomycin for injection, as part of a multi-agent combination chemotherapy regimen, is 1250 mcg/m<sup>2</sup> intravenously once every 3 weeks for 51 weeks.

## 2.4 Recommended Dosage for Metastatic Nonseminomatous Testicular Cancer

The recommended dose of dactinomycin for injection, as part of a cisplatin-based, multi-agent combination chemotherapy regimen, is 1000 mcg/m<sup>2</sup> intravenously once every 3 weeks for 12 weeks.

## 2.5 Recommended Dosage for Gestational Trophoblastic Neoplasia

The recommended dose of dactinomycin for injection for nonmetastatic and low-risk metastatic disease is 12 mcg/kg intravenously daily for five days as a single agent.

The recommended dose of dactinomycin for injection, as part of a multi-agent combination chemotherapy regimen, for high-risk metastatic disease is 500 mcg intravenously on Days 1 and 2 every 2 weeks for up to 8 weeks.

## 2.6 Recommended Dosage for Regional Perfusion in Locally Recurrent and Locoregional Solid Malignancies

The recommended dose of dactinomycin for injection, in combination with melphalan, is 50 mcg/kg once for lower extremity or pelvis.

The recommended dose of dactinomycin for injection, in combination with melphalan, is 35 mcg/kg once for upper extremity.

**Calculate the dose for obese or edematous patients based on ideal body weight.**

## 2.7 Preparation and Administration

- Dactinomycin for injection is a cytotoxic drug. Follow applicable special handling and disposal procedures.<sup>1</sup>
- Visually inspect the vials for particulate matter and discoloration, whenever solution and container permit.

### Preparation

- Reconstitute each vial by adding 1.1 mL of Sterile Water for Injection without preservative using aseptic techniques.
- The reconstituted product should be a clear, gold-colored solution at a concentration of 500 mcg/mL.
- Further dilute the reconstituted product with 5% Dextrose Injection or 0.9% Sodium Chloride Injection to yield concentrations greater than 10 mcg/mL.
- Store at room temperature for no more than 4 hours from reconstitution to completion of injection or infusion. Discard after 4 hours.
- Dactinomycin for injection does not contain a preservative. Discard any unused portions.

## Administration

- Administer the diluted reconstituted product intravenously over 10 to 15 minutes.
- Do not use in-line filters with a cellulose ester membrane.

## Management of Extravasation

- Discontinue dactinomycin for injection for burning or stinging sensation or other evidence indicating perivenous infiltration or extravasation.
- Manage confirmed or suspected extravasation as follows:
  - Terminate the injection or infusion immediately and restart in another vein.
  - Intermittent application of ice to the site for 15 minutes 4 times daily for 3 days [see *Warnings and Precautions ( 5.3)*].

## **3 DOSAGE FORMS AND STRENGTHS**

For injection: 500 mcg as a sterile, amorphous yellow to orange, lyophilized powder in a single-dose vial.

## **4 CONTRAINDICATIONS**

None.

## **5 WARNINGS AND PRECAUTIONS**

### **5.1 Secondary Malignancy or Leukemia**

The risk of developing secondary malignancies, including leukemia, is increased following treatment with dactinomycin for injection.

### **5.2 Veno-occlusive Disease**

Severe and fatal hepatic veno-occlusive disease (VOD) can occur with dactinomycin for injection. Risk factors for the development of VOD include age younger than 4 years or concomitant radiotherapy. After treatment with dactinomycin for injection, monitor frequently for signs and symptoms of VOD; these include elevations in AST, ALT, total bilirubin, hepatomegaly, weight gain, or ascites. If patients develop VOD, considering delaying next dose of dactinomycin for injection. Resume, reduce dose or permanently discontinue based on severity of reaction and disease being treated.

### **5.3 Extravasation**

Extravasation of dactinomycin for injection can result in severe local tissue injury manifesting as blistering, ulcerations and persistent pain requiring wide excision surgery followed by split-thickness skin grafting. If any signs or symptoms of extravasation occur, immediately interrupt the injection or infusion. Apply ice to the site intermittently for 15 minutes, 4 times a day for 3 days [see *Dosage and Administration ( 2.7)*]. Observe closely and consult plastic surgery if necessary based on severity of reaction.

### **5.4 Myelosuppression**

Severe and fatal myelosuppression, which may include neutropenia, thrombocytopenia and anemia, can occur with dactinomycin for injection. The nadir in neutrophil counts generally occurs 14 to 21 days after administration. Obtain complete blood counts prior to each treatment cycle. Delay next dose of dactinomycin for injection if severe myelosuppression has not improved. Consider dose reduction for patients with prolonged myelosuppression based on severity of reaction and disease being treated.

### **5.5 Immunizations**

The safety with live viral vaccines following dactinomycin for injection has not been studied and vaccination with live virus vaccines is not recommended before or during treatment.

### **5.6 Severe Mucocutaneous Reactions**

Severe mucocutaneous reactions, such as Steven-Johnson syndrome and Toxic Epidermal Necrolysis (TEN), can occur with dactinomycin for injection. Permanently discontinue dactinomycin for injection in patients who experience a severe mucocutaneous reaction.

### **5.7 Renal Toxicity**

Abnormalities of renal function can occur with dactinomycin for injection. Monitor creatinine and electrolytes frequently during dactinomycin for injection therapy.

### **5.8 Hepatotoxicity**

Hepatotoxicity can occur with dactinomycin for injection. Monitor AST, ALT, alkaline phosphatase, and bilirubin prior to and during dactinomycin for injection therapy.

### **5.9 Potentiation of Radiation Toxicity and Radiation Recall**

Dactinomycin for injection can increase radiation-induced gastrointestinal toxicity, myelosuppression, or erythema and vesiculation of the skin or buccal and pharyngeal mucosa. Reduce the dose of dactinomycin for injection by 50% during concomitant radiation.

Radiation recall, affecting previously treated radiation fields, can occur in patients who receive dactinomycin for injection after prior radiation therapy. Although the risk can occur with distant radiation exposure, the risk appears highest when dactinomycin for injection is administered within two months of prior radiation.

### **5.10 Embryo-Fetal Toxicity**

Based on findings from animal studies and its mechanism of action, dactinomycin for injection can cause fetal harm when administered to a pregnant woman. In animal reproduction studies, administration of dactinomycin to pregnant animals during the period of organogenesis was teratogenic, resulting in malformations at doses lower than the recommended human dose.

Advise pregnant women of the potential risk to the fetus. Advise females of reproductive potential to use effective contraception during treatment with dactinomycin for injection and for at least 6 months after the final dose. Advise males with female partners of reproductive potential to use effective contraception during treatment with dactinomycin for injection and for 3 months after the final dose [*see Use in Specific Populations ( 8.1, 8.3)*].

## **6 ADVERSE REACTIONS**

The following serious adverse reactions are described elsewhere in the labeling:

- Secondary Malignancy and Leukemia [*see Warnings and Precautions ( 5.1)*]
- Veno-occlusive Disease [*see Warnings and Precautions ( 5.2)*]
- Extravasation [*see Warnings and Precautions ( 5.3)*]
- Myelosuppression [*see Warnings and Precautions ( 5.4)*]
- Immunizations [*see Warning and Precautions ( 5.5)*]
- Severe Mucocutaneous Reactions [*see Warnings and Precautions ( 5.6)*]
- Renal Toxicity [*see Warnings and Precautions ( 5.7)*]
- Hepatotoxicity [*see Warnings and Precautions ( 5.8)*]
- Potentiation of Radiation Toxicity and Radiation Recall [*see Warnings and Precautions ( 5.9)*]

Common adverse reactions are: infection, alopecia, rash, dysphagia, fatigue, fever, nausea, vomiting,

anemia, neutropenia, thrombocytopenia, mucositis, and hepatotoxicity.

The following adverse reactions have been identified in clinical studies or postmarketing reports. Because some of these reactions were reported voluntarily from a population of uncertain size, it is not always possible to reliably estimate their frequency or establish a causal relationship to drug exposure.

*Infections:* infections including sepsis with fatal outcome

*Hematologic:* anemia, leukopenia, thrombocytopenia, pancytopenia, reticulocytopenia, neutropenia, febrile neutropenia, disseminated intravascular coagulation

*Immune system:* hypersensitivity

*Metabolism and nutrition:* anorexia, hypocalcemia, tumor lysis syndrome

*Nervous system:* peripheral neuropathy

*Ocular:* optic neuropathy

*Vascular:* thrombophlebitis, hemorrhage

*Respiratory, thoracic and mediastinal:* pneumonitis, pneumothorax

*Gastrointestinal:* nausea, vomiting, abdominal pain, diarrhea, constipation, gastrointestinal ulceration, cheilitis, dysphagia, esophagitis, ulcerative stomatitis, ascites, proctitis, mucositis

*Hepatobiliary:* liver function test abnormalities, hepatomegaly, hepatitis, hepatic failure with reports of death, hepatic veno-occlusive disease

*Dermatologic:* alopecia, rash, dermatitis, acne, erythema multiforme, Stevens Johnson Syndrome, radiation recall, toxic epidermal necrolysis

*Musculoskeletal and connective tissue:* myalgia, growth retardation

*Renal and urinary:* renal impairment, renal failure

*General:* fatigue, fever, malaise

## **8 USE IN SPECIFIC POPULATIONS**

### **8.1 Pregnancy**

#### Risk Summary

Based on findings from animal studies and its mechanism of action, dactinomycin for injection can cause fetal harm when administered to a pregnant woman [see *Clinical Pharmacology ( 12.1)*]. In animal reproduction studies, administration of dactinomycin to pregnant animals during the period of organogenesis was teratogenic, resulting in malformations at doses lower than the recommended human dose (see *Data*). Advise pregnant women of the potential risk to a fetus [see *Use in Special Populations ( 8.3)*].

In the U.S. general population, the estimated background risk of major birth defects and miscarriage in clinically recognized pregnancies is 2% to 4% and 15% to 20%, respectively.

#### Data

##### *Animal Data*

Dactinomycin was teratogenic in animals. Administration of dactinomycin to pregnant rats, rabbits, and hamsters during the period of organogenesis, increased the incidence of fetal malformations and caused embryotoxicity at doses (based on body surface area) as low as 0.2 times the clinical dose of 1250 mcg/m<sup>2</sup>.

### **8.2 Lactation**

## Risk Summary

There are no data on the presence of dactinomycin or its metabolites in human milk or their effects on the breastfed infant or on milk production. Because of the potential for serious adverse reactions in breastfed infants from dactinomycin for injection, advise women not to breastfeed during treatment with dactinomycin for injection and, based on limited published data regarding the dactinomycin half-life, for 14 days after the final dose.[]

### **8.3 Females and Males of Reproductive Potential**

#### Pregnancy Testing

Verify the pregnancy status of females of reproductive potential prior to initiating dactinomycin for injection [see *Use in Specific Population ( 8.1)*].

#### Contraception

Dactinomycin for injection can cause fetal harm when administered to a pregnant woman [see *Use in Specific Populations ( 8.1)*].

#### *Females*

Advise females of reproductive potential to use effective contraception during treatment with dactinomycin for injection and for at least 6 months after the final dose.

#### *Males*

Because of the potential for genotoxicity, advise males with female partners of reproductive potential to use effective contraception during treatment with dactinomycin for injection and for 3 months after the final dose [see *Nonclinical Toxicology ( 13.1)*].

### **8.4 Pediatric Use**

The safety and effectiveness of dactinomycin have been established in pediatric patients with Wilms tumor, rhabdomyosarcoma, Ewing sarcoma, and metastatic nonseminomatous testicular cancer .

The safety and effectiveness of dactinomycin have been established in post-menarchal pediatric patients with gestational trophoblastic neoplasia.

The safety and effectiveness of dactinomycin for injection have not been established in pediatric patients undergoing regional perfusion for locally recurrent or locoregional solid malignancies.

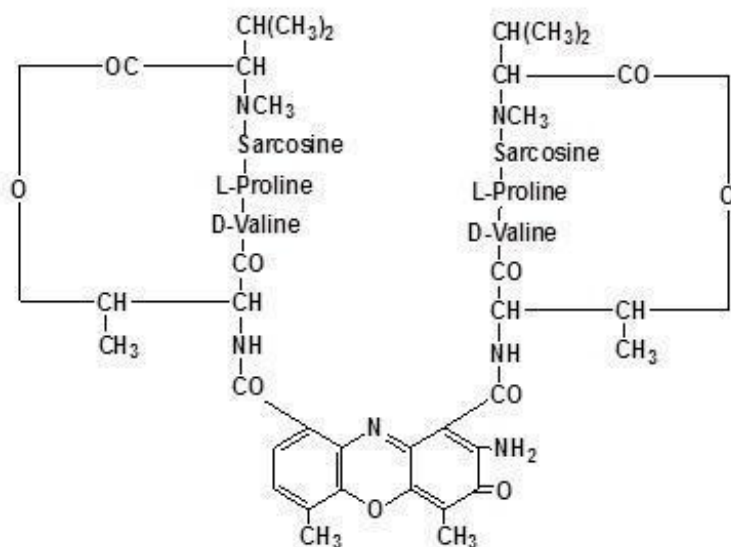
### **8.5 Geriatric Use**

Clinical studies of dactinomycin for injection did not include sufficient numbers of subjects aged 65 and over to determine whether they respond differently from younger subjects.

## **11 DESCRIPTION**

Dactinomycin is an actinomycin. Dactinomycin is produced by *Streptomyces parvullus*. The chemical name is 8-amino-N-(2-amino-4,6-dimethyl-3-oxo-phenoxazin-1-yl)carbonyl-N'-[8-amino-4,6-dimethyl-7-oxo-9-[[3,6,10-trimethyl-7,14-bis(1-methylethyl)-2,5,8,12,15-pentaoxo-9-oxa-3,6,13,16-tetrazabicyclo[14.3.0]nonadec-11-yl]carbamoyl]phenoxazin-1-yl]carbonyl-4,6-dimethyl-7-oxo-N,N'-bis[3,6,10-trimethyl-7,14-bis(1-methylethyl)-2,5,8,12,15-pentaoxo-9-oxa-3,6,13,16-tetrazabicyclo[14.3.0]nonadec-11-yl]-1,9-bis[[3,6,10-trimethyl-7,14-bis(1-methylethyl)-2,5,8,12,15-pentaoxo-9-oxa-3,6,13,16-tetrazabicyclo[14.3.0]nonadec-11-yl]carbamoyl]phenoxazine-1,9-dicarboxamide. The molecular formula is C<sub>62</sub>H<sub>86</sub>N<sub>12</sub>O<sub>16</sub> and the molecular weight is 1255.42 daltons. The structural formula of dactinomycin is shown below:





Dactinomycin for Injection USP for intravenous use is a sterile, amorphous yellow to orange, lyophilized powder in a single-dose vial. Each vial contains 500 mcg of dactinomycin and 20 mg of mannitol.

## 12 CLINICAL PHARMACOLOGY

### 12.1 Mechanism of Action

Dactinomycin for injection is a cytotoxic actinomycin that binds DNA and inhibits RNA synthesis. The cytotoxic activity of dactinomycin has been demonstrated in animal models of different human cancers.

### 12.2 Pharmacodynamics

Dactinomycin exposure-response relationships and the time course of pharmacodynamics response are unknown.

### 12.3 Pharmacokinetics

The distribution and excretion of radiolabeled dactinomycin ( $^3\text{H}$  actinomycin D) were assessed in three adult patients with malignant melanoma.

#### Distribution

$^3\text{H}$  actinomycin D is concentrated in nucleated cells and does not penetrate the blood-brain barrier.

#### Elimination

##### *Excretion*

Following administration of radiolabeled dactinomycin, approximately 30% was recovered in urine and feces in one week.

#### Specific Populations

##### *Pediatric Patients*

Published studies and population analyses in patients  $\leq 21$  years of age with cancer report a trend of increasing systemic dactinomycin clearance with increasing body weight.

#### Drug Interaction Studies

Published in vitro studies report that dactinomycin may be a substrate of the P-glycoprotein and OATP1B3 transporter systems.

## 13 NONCLINICAL TOXICOLOGY

### 13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility

Dactinomycin is a carcinogen in animals. Local sarcomas were produced in mice and rats after repeated subcutaneous or intraperitoneal injections. Mesenchymal tumors occurred in male rats given intraperitoneal injections of 50 mcg/kg, 2 to 5 times per week, for 18 weeks, at doses (based on body surface area) 0.5 times the clinical dose of 1250 mcg/m<sup>2</sup>.

Dactinomycin was mutagenic in several in vitro and in vivo test systems including human fibroblasts and leukocytes, and HeLa cells. DNA damage and cytogenetic effects have been demonstrated in the mouse and the rat.

## 15 REFERENCES

1. "OSHA Hazardous Drugs." OSHA. <http://www.osha.gov/SLTC/hazardousdrugs/index.html>

## 16 HOW SUPPLIED/STORAGE AND HANDLING

Dactinomycin for Injection USP for intravenous use is supplied as a sterile, amorphous yellow to orange, lyophilized powder in a single-dose vial. Each Dactinomycin for Injection USP vial (NDC 42658-008-01) contains 0.5 mg of dactinomycin and 20 mg of mannitol.

Store at 20 to 25°C (68 to 77°F); excursions permitted between 15 to 30°C (59 to 86°F) [see USP Controlled Room Temperature].

Protect Dactinomycin for Injection USP from light and humidity.

Store the reconstituted Dactinomycin for Injection USP at room temperature for no more than 4 hours from reconstitution to completion of administration [see *Dosage and Administration* ( 2.7)] .

Dactinomycin for Injection USP is a cytotoxic drug. Follow applicable special handling and disposal procedures. <sup>1</sup>

## 17 PATIENT COUNSELING INFORMATION

### Secondary Malignancy or Leukemia

Advise patients of the increased risk of secondary malignancies [see *Warnings and Precautions* ( 5.1)] .

### Veno-occlusive Disease

Advise patients about the symptoms of VOD and to seek medical attention if they develop new onset jaundice, abdominal distention, or right upper quadrant pain [see *Warnings and Precautions* ( 5.2)] .

### Myelosuppression

Advise patients to contact their healthcare provider for any signs or symptoms of myelosuppression or infection [see *Warnings and Precautions* ( 5.4)] .

### Severe Mucocutaneous Reactions

Advise patients of the risk of severe mucocutaneous reactions and to contact their health care provided for new skin lesions, mouth sores or oropharyngeal lesions [see *Warnings and Precautions* ( 5.5)] .

### Renal Toxicity or Hepatotoxicity

Advise patients of the need for periodic laboratory testing to monitor for renal toxicity and hepatotoxicity [see *Warnings and Precautions* ( 5.7, 5.8)] .

### Potentiation of Radiation Toxicity and Radiation Recall

Advise patients of the risk of increased radiation-induced gastrointestinal, myelosuppression and skin toxicity [see Warnings and Precautions ( 5.9)] .

#### Embryo-Fetal Toxicity

Advise females of reproductive potential of the potential risk to a fetus. Advise females to inform their healthcare provider of a known or suspected pregnancy [see Warnings and Precautions ( 5.10), Use in Specific Populations ( 8.1)] .

Advise females of reproductive potential to use effective contraception during treatment with dactinomycin for injection and for 6 months after final dose [see Use in Specific Populations ( 8.3)] .

Advise male patients with female partners of reproductive potential to use effective contraception during treatment with dactinomycin for injection and for 3 months after final dose [see Use in Specific Populations ( 8.3)] .

#### Lactation

Advise females not to breastfeed during treatment with dactinomycin for injection and for 14 days after the final dose [see Use in Specific Populations ( 8.2)] .

Distributed by:

Hisun Pharmaceuticals USA, Inc.

Bridgewater, NJ 08807 USA

Manufactured in China

#### **PACKAGE/LABEL PRINCIPAL DISPLAY PANEL**

NDC 42658- 008-01 Vial Label

**Dactinomycin for injection, USP**

500 mcg per vial

**For Preparation of Intravenous Solutions**  
Reconstitute by adding 1.1 mL of Sterile Water for Injection (without preservative).  
Store at 20° to 25°C (68° to 77°F) [see USP Controlled Room Temperature].  
Protect from light and humidity.  
Distributed By:  
Hisun Pharmaceuticals USA, Inc.  
Bridgewater, NJ 08807 USA  
Manufactured in China    Rev. 07/18

NDC 42658-008-01

**Dactinomycin for Injection, USP**

**500 mcg per vial**

**Caution: Cytotoxic Agent**

Rx only    Single-Dose Vial

 **HISUNUSA**

  
N 3 42658 00801 5

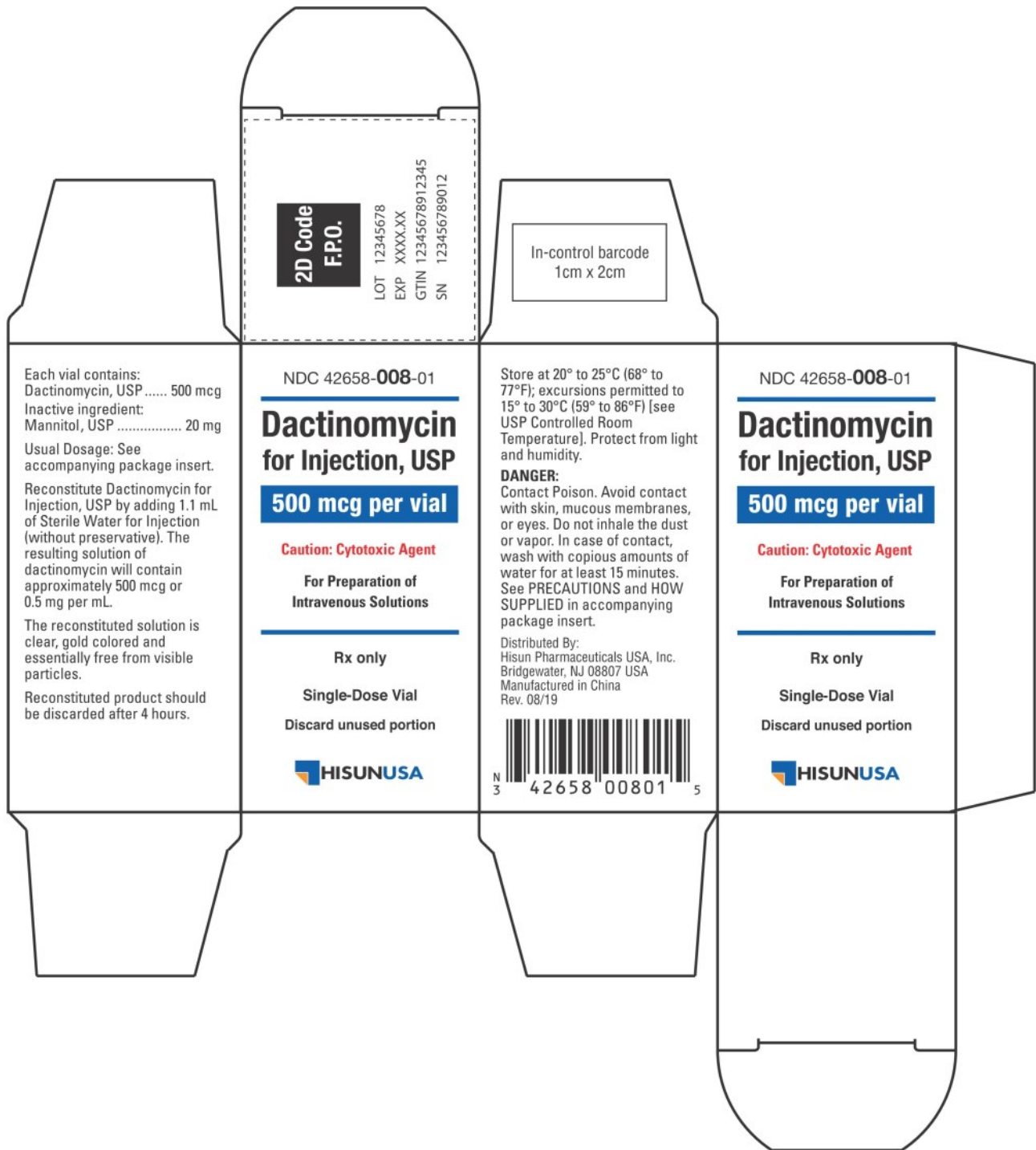
LOT    EXP.

In-control barcode  
3mm x 6mm

NDC 42658- 008-01 Inner carton

**Dactinomycin for injection, USP**

500 mcg per vial



## DACTINOMYCIN

dactinomycin injection, powder, lyophilized, for solution

### Product Information

<b>Product Type</b>	HUMAN PRESCRIPTION DRUG	<b>Item Code (Source)</b>	NDC:42658-008
<b>Route of Administration</b>	INTRAVENOUS		

**Active Ingredient/Active Moiety**

Ingredient Name	Basis of Strength	Strength
DACTINOMYCIN (UNII: 1CC1JFE158) (DACTINOMYCIN - UNII:1CC1JFE158)	DACTINOMYCIN	0.5 mg

**Inactive Ingredients**

Ingredient Name	Strength
MANNITOL (UNII: 3OWL53L36A)	20 mg

**Packaging**

#	Item Code	Package Description	Marketing Start Date	Marketing End Date
1	NDC:42658-008-01	1 in 1 CARTON	01/01/2021	
1		1 in 1 VIAL; Type 0: Not a Combination Product		

**Marketing Information**

Marketing Category	Application Number or Monograph Citation	Marketing Start Date	Marketing End Date
ANDA	ANDA207232	01/01/2021	

**Labeler** - Hisun Pharmaceuticals USA, Inc. (961628505)**Establishment**

Name	Address	ID/FEI	Business Operations
Hisun Pharmaceutical (Hangzhou) Co., Ltd.		421250870	api manufacture(42658-008) , manufacture(42658-008) , analysis(42658-008) , label(42658-008) , pack(42658-008)

Revised: 9/2020

Hisun Pharmaceuticals USA, Inc.