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MATERIAL SAFETY DATA SHEET

Schering-Plough urges each user or recipient of this MSDS to read the entire data sheet to become aware of the hazards associated with this material.

SECTION 1. IDENTIFICATION OF SUBSTANCE AND CONTACT INFORMATION

MSDS NAME: Doxorubicin Hydrochloride Liposome Injection [Formulation]
SYNONYM(S): CAELYX (pegylated liposomal doxorubicin hydrochloride)
Doxil
Doxorubicin Hydrochloride (SCH 200746)
MSDS NUMBER: SP000109
EMERGENCY NUMBER(S): Schering-Plough Security Control Center (908) 820-6921 (24 Hours)
Transportation Emergencies - CANUTEC:
(613) 996-6666 (Canada)
SCHERING-PLOUGH MSDS HELPLINE: (800) 770-8878 (US and Canada)
(908) 473-3371 (Worldwide)
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SECTION 2. HAZARDS IDENTIFICATION

EMERGENCY OVERVIEW

Liquid
Red
Odor unknown

May be irritating to skin, eyes, or mucous membranes.
May cause reproductive effects.
May cause impaired fertility.
May be harmful if absorbed through skin or if swallowed.
May cause cancer.
May be a mutagen.

Causes effects to:
skin
endocrine system

May cause effects to:
bone marrow
brain
cardiovascular system
central nervous system
fetus
immune system
kidney
liver
reproductive system
spleen

MSDS NUMBER: SP000109

SECTION 2. HAZARDS IDENTIFICATION

POTENTIAL HEALTH EFFECTS:

Doxorubicin hydrochloride is a cytotoxic anthracycline antibiotic that can cause cardiac toxicity, myelosuppression (inhibition of blood cell production), bone marrow suppression, and anemia. Adverse reactions have included changes in blood cell counts (neutropenia, general anemia, and thrombocytopenia), hand and foot syndrome (palmar-plantar skin eruptions).

Doxorubicin hydrochloride in animal studies caused tumors, immunosuppression, cardiotoxicity, myelosuppression and reproductive effects including testicular atrophy in rats and dogs.

LISTED CARCINOGENS

CHEMICAL NAME	CAS NUMBER	OSHA	IARC	NTP	ACGIH
Doxorubicin hydrochloride.	25316-40-9			Anticipated carcinogen.	

Doxorubicin and doxorubicin hydrochloride are listed as NTP Group 2B (anticipated) carcinogens. Doxorubicin is also listed as an IARC Group 2A carcinogen (probably carcinogenic to humans).

SECTION 3. COMPOSITION AND INFORMATION ON INGREDIENTS

PRODUCT USE: Drug product

CHEMICAL FORMULA: Mixture.

The formulation for this product is proprietary information. Only hazardous ingredients in concentrations of 1% or greater and/or carcinogenic ingredients in concentrations of 0.1% or greater are listed in the Chemical Composition table. Active ingredients in any concentration are listed. For additional information about carcinogenic ingredients see Section 2.

CHEMICAL COMPOSITION

CHEMICAL NAME	CAS NUMBER	PERCENT
Doxorubicin hydrochloride.	25316-40-9	0.2
Liposomal carrier.	Mixture	99.8

ADDITIONAL INFORMATION:

This MSDS is written to provide health and safety information for individuals who will be handling the final product formulation during research, manufacturing, and distribution. For health and safety information for individual ingredients used during manufacturing, refer to the appropriate MSDS for each ingredient. Refer to the package insert or product label for handling guidance for the consumer.

SECTION 4. FIRST AID MEASURES

INHALATION:

Remove to fresh air. If any trouble breathing, get immediate medical attention. Administer artificial respiration if breathing has ceased. If irritation or symptoms occur or persist, consult a physician.

SKIN CONTACT:

In case of skin contact, while wearing protective gloves, carefully remove any contaminated clothing, including shoes, and wash skin thoroughly with soap and water. If irritation or symptoms occur or persist, consult a physician.

EYE CONTACT:

In case of eye contact, immediately rinse eyes thoroughly with plenty of water. If wearing contact lenses, remove only after initial rinse, and continue rinsing eyes for at least 15 minutes. If irritation occurs or persists, consult a physician.

INGESTION:

Rinse mouth and drink a glass of water. Do not induce vomiting unless under the direction of a qualified medical professional or Poison Control Center. If symptoms persist, consult a physician.

SECTION 5. FIRE FIGHTING MEASURES

FLAMMABILITY DATA:

Doxorubicin Hydrochloride Liposome Injection
[Formulation]
Latest Revision Date: 21-Mar-2008

SECTION 5. FIRE FIGHTING MEASURES

Flash Point:

Not determined (liquids) or not applicable (solids).

SPECIAL FIRE FIGHTING PROCEDURES:

Wear full protective clothing and self-contained breathing apparatus (SCBA).

SUITABLE EXTINGUISHING MEDIA:

Carbon dioxide (CO₂), extinguishing powder or water spray.

See Section 9 for Physical and Chemical Properties.

SECTION 6. ACCIDENTAL RELEASE MEASURES

PERSONAL PRECAUTIONS:

Wear appropriate personal protective equipment as specified in Section 8. Keep personnel away from the clean-up area.

SPILL RESPONSE / CLEANUP:

All spills should be handled according to site requirements and based on precautions cited in the MSDS. In the case of liquids, use proper absorbent materials. For laboratories and small-scale operations, incidental spills within a hood or enclosure should be cleaned by using a HEPA filtered vacuum or wet cleaning methods as appropriate. For large dry or liquid spills or those spills outside enclosure or hood, appropriate emergency response personnel should be notified. In manufacturing and large-scale operations, HEPA vacuuming prior to wet mopping or cleaning is required.

See Sections 9 and 10 for additional physical, chemical, and hazard information.

SECTION 7. HANDLING AND STORAGE

HANDLING:

Keep containers adequately sealed during material transfer, transport, or when not in use.

Appropriate handling of this material is dependent on many factors, including physical form, duration and frequency of process or task, and effectiveness of engineering controls. Site-specific risk assessments should be conducted to determine the feasibility and the appropriateness of all exposure control measures. See Section 8 (Exposure Controls) for additional guidance.

STORAGE:

Store in a cool, dry, well ventilated area.

See Section 8 for exposure controls and additional safe handling information.

SECTION 8. EXPOSURE CONTROLS AND PERSONAL PROTECTION

The following guidance applies to the handling of the active ingredient(s) in this formulation.

S-P HEALTH HAZARD CATEGORY (HHC):

The Schering-Plough Health Hazard Category (HHC) for this material is HHC3. Materials in this category are considered high health hazards. Typical occupational exposure limits for materials in this category range between 10-50 mcg/m³ (8-hr TWA). Health Hazard Categories are intended to be a component of workplace risk assessment. Consult your site safety and industrial hygiene staff for guidance on handling and control strategies.

EXPOSURE CONTROLS:

The health hazard risks of handling this material are dependent on many factors, including physical form, duration and frequency of process or task, and effectiveness of engineering controls. Site-specific risk assessments should be conducted to determine the feasibility and the appropriateness of all exposure control measures. Exposure controls for normal operating or routine procedures follow a tiered strategy. Engineering controls are the preferred means of long-term or permanent exposure control. If engineering controls are not feasible, appropriate use of personal protective equipment (PPE) may be considered as alternative control measures. Exposure controls for non-routine operations must be evaluated and addressed as part of the site-specific risk assessment.

RECOMMENDED PERSONAL PROTECTIVE EQUIPMENT (PPE):

Respiratory Protection:

Respiratory protective equipment (RPE) may be required for certain laboratory and large-scale manufacturing tasks if potential airborne breathing zone concentrations of substances exceed the relevant exposure limit(s). Workplace risk assessment should be completed before specifying and implementing RPE usage. Potential exposure points and pathways, task duration and frequency, potential employee contact with the substance, and the ability of the substance to be rendered airborne during specific tasks should be evaluated. Initial and ongoing strategies of quantitative exposure measurement should be obtained as required by the workplace risk assessment. All RPE must conform to local and regional specifications for efficacy and performance. Consult your site or corporate health and safety professional for additional guidance.

Skin Protection:

Gloves that provide an appropriate barrier to the skin are recommended if there is potential for contact with this material. Consult your site safety staff for guidance.

Eye Protection:

Safety glasses with side shields. Use of goggles or full face protection may be required based on hazard, potential for contact, or level of exposure. Consult your site safety staff for guidance.

Body Protection:

In small-scale or laboratory operations, lab coats or equivalent protection is required. Disposable Tyvek or other dust impermeable suit should be considered based on procedure or level of exposure. Use of additional PPE such as shoe coverings, gauntlets, hood, or head covering may be necessary. Consult your site safety staff for guidance.

In large-scale or manufacturing operations, disposable Tyvek or other dust impermeable suit is recommended and based on level of exposure. Use of additional PPE such as shoe coverings, gauntlets, hood, or head covering may be necessary. Consult your site safety staff for guidance.

EXPOSURE LIMIT VALUES

No exposure limits are available for the active ingredient(s) or any other hazardous ingredient in this formulation.

SECTION 9. PHYSICAL AND CHEMICAL PROPERTIES

FORM: Liquid
COLOR: Red
ODOR: Odor unknown
pH: 6.5
SPECIFIC GRAVITY: 1.03
SOLUBILITY: Soluble
Water:

See Section 5 for flammability/explosivity information.

SECTION 10. STABILITY AND REACTIVITY

STABILITY/ REACTIVITY:
Stable under normal conditions.

INCOMPATIBLE MATERIALS / CONDITIONS TO AVOID:
None known.

SECTION 11. TOXICOLOGICAL INFORMATION

The information presented pertains to the following individual ingredients of this material and not to the formulated product.

ACUTE TOXICITY DATA

PRODUCT / CHEMICAL NAME	EXPOSURE ROUTE	STUDY DESCRIPTION	RESULT
Doxorubicin hydrochloride	Oral	LD50 (mouse)	570-698 mg/kg

SKIN:
Moderately irritating.

EYE:
Moderately irritating.

Doxorubicin Hydrochloride Liposome Injection
[Formulation]
Latest Revision Date: 21-Mar-2008

REPEAT DOSE TOXICITY DATA

SUBCHRONIC / CHRONIC TOXICITY:

Doxorubicin hydrochloride: Studies (2 days to 14 weeks) were performed in rats, mice, rabbits, and dogs. Dosages of 2 to 60 mg/kg/day were given primarily via intraperitoneal and intravenous injections. Effects seen were Electro-Kardio-Graph changes, arrhythmias, bone marrow impact, heart, liver, spleen, thymus, testicular weight changes, leukopenia, normocytic anemia and death.

REPRODUCTIVE / DEVELOPMENTAL TOXICITY:

Doxorubicin hydrochloride: Rats, mice, and rabbits were given injections (IP, IV, subcutaneous) of 1 to 60 mg/kg/day. Effects included changes to the testes, epididymis, sperm ducts, ovaries, fallopian tubes, fertility index, spermatogenesis, prostate and seminal vesicles.

MUTAGENICITY / GENOTOXICITY:

Doxorubicin hydrochloride has been shown to be positive in a wide variety of genotoxicity, in-vivo and in-vitro, studies.

Liposomal carrier was negative in Ames, mouse lymphoma, chromosomal aberration assays, and mammalian micronucleus assay.

CARCINOGENICITY:

Doxorubicin hydrochloride produced mammary tumors in rats after intravenous and subcutaneous injections. Intravesicular instillation in rats resulted in low incidence of bladder papillomas and increased the incidence of induced bladder tumors.

SECTION 12. ECOLOGICAL INFORMATION

ECOTOXICITY DATA

There are no ecotoxicity data available for this product or its components.

ENVIRONMENTAL DATA

There are no environmental data available for this product or its components.

SECTION 13. DISPOSAL CONSIDERATIONS

MATERIAL WASTE:

Disposal must be in accordance with applicable federal, state/provincial, and/or local regulations. Incineration is the preferred method of disposal, when appropriate. Operations that involve the crushing or shredding of waste materials or returned goods must be handled to meet the recommended exposure limit(s).

PACKAGING AND CONTAINERS:

Disposal must be in accordance with applicable federal, state/provincial, and/or local regulations.

SECTION 14. TRANSPORT INFORMATION

This material is not subject to the transportation regulations of DOT, IATA, IMO, and the ADR.

SECTION 15. REGULATORY INFORMATION

WHMIS CLASSIFICATIONS:

This product has been classified in accordance with the hazard criteria on the Controlled Products Regulations and the MSDS contains all the information required by the Controlled Products Regulations. The final packaged product is not subject to WHMIS classification. The following classification applies to the bulk formulation handled in the workplace.

Controlled Product Class: D2A: Very Toxic



TSCA LISTING

This material or product is not subject to TSCA requirements.

SECTION 16. OTHER INFORMATION

Although reasonable care has been taken in the preparation of this document, we extend no warranties and make no representations as to the accuracy or completeness of the information contained therein, and assume no responsibility regarding the suitability of this information for the user's intended purposes or for the consequence of its use. Each individual should make a determination as to the suitability of the information for their particular purpose(s).

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