SECTION 1. IDENTIFICATION

Substance name: DOXIL
CAELYX
Pegylated liposomal doxorubicin hydrochloride

Manufacturer or supplier's details
Company name of supplier: Janssen Pharmaceuticals, Inc.
Address: 1125 Trenton-Harborton Rd
Titusville NJ 08560
US
Telephone: (609) 730-2000

Emergency telephone number: +32 14 60 24 44
E-mail address Responsible/issuing person: SDSJanssen@its.jnj.com

Recommended use of the chemical and restrictions on use
Recommended use: Finished Pharmaceutical Product
Pharmacotherapeutic group: Cytostatics
This SDS is only intended for occupational use and not for consumer use (see patient packaging insert for consumer use). This SDS is written to provide environmental, health and safety information for personnel that will be handling this finished pharmaceutical product. For health and safety information during manufacturing of this product we refer to the appropriate SDS for each component.
This dosage form is not exempt from the requirements of the OSHA Hazard Communication Standard (US OSHA Standard 29 CFR Part 1910.1200).

SECTION 2. HAZARDS IDENTIFICATION

GHS Classification
Acute toxicity: Category 4
Skin corrosion/irritation: Category 2
Serious eye damage/eye irritation: Category 1
Specific target organ toxicity - single exposure: Category 3
Carcinogenicity: Category 1B
Reproductive toxicity: Category 2
SAFETY DATA SHEET

Medicinal products in the finished state, intended for the final user, are not subject to GHS labeling.

Hazard pictograms:

- \[\text{Signal word} : \text{Danger} \]

Hazard statements:
- H361fd Suspected of damaging fertility. Suspected of damaging the unborn child.
- H350 May cause cancer.
- H302 Harmful if swallowed.
- H315 Causes skin irritation.
- H318 Causes serious eye damage.
- H335 May cause respiratory irritation.

Precautionary statements:
- **Prevention:**
  - P202 Do not handle until all safety precautions have been read and understood.
  - P280 Wear protective gloves/ eye protection/ face protection.
  - P271 Use only outdoors or in a well-ventilated area.
  - P264 Wash hands thoroughly after handling.
  - P270 Do not eat, drink or smoke when using this product.
- **Response:**
  - P310 Immediately call a POISON CENTER or doctor/ physician.
  - P321 Specific treatment (see supplemental first aid instructions on this label).
  - P304 + P340 IF INHALED: Remove victim to fresh air and keep at rest in a position comfortable for breathing.
  - P302 + P352 IF ON SKIN: Wash with plenty of soap and water.
  - P305 + P351 + P338 IF IN EYES: Rinse cautiously with water for several minutes. Remove contact lenses, if present and easy to do. Continue rinsing.
  - P301 + P312 IF SWALLOWED: Call a POISON CENTER or doctor/ physician if you feel unwell.
  - P330 Rinse mouth.
- **Storage:**
  - P403 + P233 Store in a well-ventilated place. Keep container tightly closed.
  - P405 Store locked up.
- **Disposal:**
  - P501 Dispose of contents/ container to an approved waste disposal plant.

Other hazards:
Refer to the pharmacotherapeutic group (section 1.2) and the patient packaging insert to evaluate the possible workplace hazards when this Finished Pharmaceutical Product is accidently leaking, broken or crushed.

SECTION 3. COMPOSITION/INFORMATION ON INGREDIENTS

Substance / Mixture : Mixture
Chemical nature : Liquid

Hazardous components

<table>
<thead>
<tr>
<th>Chemical Name</th>
<th>CAS-No.</th>
<th>Concentration (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>DOXORUBICIN HYDROCHLORIDE</td>
<td>25316-40-9</td>
<td>&gt;= 0.1 - &lt; 1</td>
</tr>
</tbody>
</table>

SECTION 4. FIRST AID MEASURES

If inhaled : If breathed in, move person into fresh air. Consult a physician.

In case of skin contact : Take off contaminated clothing and shoes immediately. Wash off immediately with plenty of water. If symptoms persist, call a physician. Wash contaminated clothing before re-use.

In case of eye contact : Rinse immediately with plenty of water, also under the eyelids, for at least 15 minutes. Remove contact lenses. Consult a physician.

If swallowed : Rinse mouth with water. Call a physician immediately.

Most important symptoms and effects, both acute and delayed : Ingestion may provoke the following symptoms: Harmful if swallowed. Danger of very serious irreversible effects. Consult the patient packaging insert for more information about this Finished Pharmaceutical Product.

Notes to physician : Treat symptomatically. Consult the patient packaging insert for more information about this Finished Pharmaceutical Product.

SECTION 5. FIREFIGHTING MEASURES

Suitable extinguishing media : Use extinguishing measures that are appropriate to local circumstances and the surrounding environment.

Unsuitable extinguishing media : Water spray jet

Hazardous combustion products : No hazardous combustion products are known

Further information : In the event of fire, cool tanks with water spray.

Special protective equipment for firefighters : In the event of fire, wear self-contained breathing apparatus.
SECTION 6. ACCIDENTAL RELEASE MEASURES

Personal precautions, protective equipment and emergency procedures: Evacuate personnel to safe areas. In the event of an accidental release the emergency response team must respond based on a risk assessment and use personal protective equipment as appropriate.

Environmental precautions: Should not be released into the environment.

Methods and materials for containment and cleaning up: Large spills: Dam up. Soak up with inert absorbent material. Keep in properly labelled containers. Small spills: Gently cover the spill with an absorbent towel or pad. Large spills + Small spills: Keep in suitable, closed containers for disposal. Treat recovered material as described in the section “Disposal considerations”.

SECTION 7. HANDLING AND STORAGE

Advice on protection against fire and explosion: No data available

Advice on safe handling: To avoid thermal decomposition, do not overheat. For personal protection see section 8. Avoid inhalation, ingestion and contact with skin and eyes. Do not break, crush or spill this Finished Pharmaceutical Product.

Conditions for safe storage: To maintain product quality, do not store in heat or direct sunlight. Store in original container. Keep containers tightly closed in a dry, cool and well-ventilated place. Keep away from heat and sources of ignition. Keep locked up.

Recommended storage temperature: 2 - 8 °C

SECTION 8. EXPOSURE CONTROLS/PERSONAL PROTECTION

Components with workplace control parameters

<table>
<thead>
<tr>
<th>Components</th>
<th>CAS-No.</th>
<th>Value type (Form of exposure)</th>
<th>Control parameters / Permissible concentration</th>
<th>Basis</th>
</tr>
</thead>
<tbody>
<tr>
<td>DOXORUBICIN HYDROCHLORIDE</td>
<td>25316-40-9</td>
<td>TWA</td>
<td>0.00047 mg/m3</td>
<td>J&amp;J OEL/PBOEL HHC</td>
</tr>
<tr>
<td></td>
<td></td>
<td>PBOEL-HHC</td>
<td>4</td>
<td>J&amp;J OEL/PBOEL</td>
</tr>
</tbody>
</table>
Further information: J&J has a hazard banding notation: PBOEL HHC. This substance is classified by J&J as being PBOEL HHC 4. Notation CAR: carcinogenic properties, Notation REPRO: has the potential to have adverse effects on reproduction and fetal development.

**Engineering measures**

All personal protective equipment should be based on a risk assessment. Consult a Environment Health Safety expert if necessary.

**Personal protective equipment**

**Respiratory protection**

No personal respiratory protective equipment normally required. Engineering controls should always be the primary method of controlling exposures. If respiratory protective equipment is needed for certain activities, the type as well as the corresponding protection factor will depend upon the risk assessment and air concentrations, hazards, physical and warning properties of substances present.

**Hand protection**

Remarks: Skin protection required for pregnant women or women of child bearing age. Gloves

**Skin and body protection**

Preventive skin protection

**Protective measures**

The type of protective equipment must be selected based on the Environmental Health and Safety risk assessment. Consult a Environmental Health and Safety expert if necessary.

**Hygiene measures**

Handle in accordance with good industrial hygiene and safety practice.

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**SECTION 9. PHYSICAL AND CHEMICAL PROPERTIES**

**Appearance**

Vial

**Colour**

red

**Odour**

No data available

**Odour Threshold**

No data available

**pH**

No data available

**Melting point/range**

No data available

**Boiling point/boiling range**

No data available

**Flash point**

No data available
SAFETY DATA SHEET

Upper explosion limit : No data available
Lower explosion limit : No data available
Vapour pressure : No data available
Relative vapour density : No data available
Relative density : No data available
Density : No data available
Solubility(ies)  
Water solubility : No data available
Partition coefficient: n-octanol/water : No data available
Decomposition temperature : No data available
Viscosity  
Viscosity, dynamic : No data available
Viscosity, kinematic : No data available
Explosive properties : No data available
Conductivity : No data available
Molecular weight : 579.99 g/mol

SECTION 10. STABILITY AND REACTIVITY

Reactivity : None reasonably foreseeable.
Chemical stability : Stable under recommended storage conditions.
Possibility of hazardous reactions : No dangerous reaction known under conditions of normal use.
Conditions to avoid : To avoid thermal decomposition, do not overheat.
Incompatible materials : None known.
Hazardous decomposition products : None known.

SECTION 11. TOXICOLOGICAL INFORMATION

Acute toxicity
Product:
Acute oral toxicity: LD50 (Mouse): 698 mg/kg
  Assessment: The component/mixture is moderately toxic after single ingestion.

Components:
DOXORUBICIN HYDROCHLORIDE
  Acute oral toxicity: LD50 (Mouse): 570 mg/kg
  Assessment: The component/mixture is moderately toxic after single ingestion.

Acute inhalation toxicity: Remarks: No data available

Acute dermal toxicity: Remarks: No data available

Acute toxicity (other routes of administration): Remarks: No data available

Skin corrosion/irritation

Product:
Result: Skin irritation

Components:
DOXORUBICIN HYDROCHLORIDE
Remarks: No data available

Serious eye damage/eye irritation

Product:
Result: Corrosive to eyes

Components:
DOXORUBICIN HYDROCHLORIDE
Result: Eye irritation

Result: Lachrymation

Respiratory or skin sensitisation

Components:
DOXORUBICIN HYDROCHLORIDE
Remarks: No data available

Germ cell mutagenicity

Components:
DOXORUBICIN HYDROCHLORIDE
Genotoxicity in vitro: Remarks: No data available

Germ cell mutagenicity: Animal experiments showed mutagenic and teratogenic
Carcinogenicity

Components:

DOXORUBICIN HYDROCHLORIDE

Remarks: carcinogenic effects

Carcinogenicity - Assessment: Sufficient evidence of carcinogenicity in animal experiments

IARC

No component of this product present at levels greater than or equal to 0.1% is identified as probable, possible or confirmed human carcinogen by IARC.

Group 3: Not classifiable as to its carcinogenicity to humans

CHOLESTEROL 57-88-5

OSHA

No component of this product present at levels greater than or equal to 0.1% is identified as a carcinogen or potential carcinogen by OSHA.

NTP

No component of this product present at levels greater than or equal to 0.1% is identified as a known or anticipated carcinogen by NTP.

Reproductive toxicity

Components:

DOXORUBICIN HYDROCHLORIDE

Effects on fertility:

Remarks: No data available

Effects on foetal development:

Species: Rat

Remarks: Did show teratogenic effects in animal experiments.

Teratogenicity - Assessment:

Potential embryo-foetal toxicity and teratogenicity., Limited evidence of adverse effects on development in animal studies and/or human studies.

STOT - single exposure

Product:

Assessment: The substance or mixture is classified as specific target organ toxicant, single exposure, category 3 with respiratory tract irritation.

Components:

DOXORUBICIN HYDROCHLORIDE

Remarks: No data available
STOT - repeated exposure
No data available

Repeated dose toxicity

Components:
DOXORUBICIN HYDROCHLORIDE
Remarks: No data available

Aspiration toxicity
No data available

SECTION 12. ECOLOGICAL INFORMATION

Ecotoxicity

Components:
DOXORUBICIN HYDROCHLORIDE

Toxicity to fish:
LC50 (Danio rerio (zebra fish)): 68 mg/l
Exposure time: 96 h
Method: OECD Test Guideline 203

NOEC (Danio rerio (zebra fish)): 46 mg/l
Exposure time: 96 h
Method: OECD Test Guideline 203

Toxicity to daphnia and other aquatic invertebrates:
EC50 (Daphnia magna (Water flea)): 1.8 mg/l
Exposure time: 48 h
Method: OECD Test Guideline 202
Remarks: No data available

NOEC (Daphnia magna (Water flea)): 0.07 mg/l
Exposure time: 48 h
Method: OECD Test Guideline 202

Toxicity to algae:
ErC50 (Pseudokirchneriella subcapitata (microalgae)): 11 mg/l
Exposure time: 72 h
Test Type: Growth inhibition
Method: OECD Test Guideline 201
Remarks: No data available

NOECr (Pseudokirchneriella subcapitata (microalgae)): 1.9 mg/l
Exposure time: 72 h
Test Type: Growth inhibition
Method: OECD Test Guideline 201

EbC50 (Pseudokirchneriella subcapitata (microalgae)): 4.1 mg/l
Exposure time: 72 h
Test Type: Cell multiplication inhibition test
Method: OECD Test Guideline 201
NOECb (Pseudokirchneriella subcapitata (microalgae)): 1.9 mg/l
Exposure time: 72 h
Test Type: Cell multiplication inhibition test
Method: OECD Test Guideline 201

Toxicity to bacteria: EC50 (activated sludge): > 1,000 mg/l
Exposure time: 3 h
Method: OECD Test Guideline 209

NOEC (activated sludge): 246 mg/l
Exposure time: 3 h
Method: OECD Test Guideline 209

Persistence and degradability

Components:
DOXORUBICIN HYDROCHLORIDE
Biodegradability: Remarks: No data available

Bioaccumulative potential

Components:
DOXORUBICIN HYDROCHLORIDE
Bioaccumulation: Remarks: No data available
Partition coefficient: n-octanol/water: Remarks: No data available

Mobility in soil
No data available

Other adverse effects

Product:
Ozone-Depletion Potential: Regulation: 40 CFR Protection of Environment; Part 82
Protection of Stratospheric Ozone - CAA Section 602 Class I Substances
Remarks: This product neither contains, nor was manufactured with a Class I or Class II ODS as defined by the U.S. Clean Air Act Section 602 (40 CFR 82, Subpt. A, App.A + B).

SECTION 13. DISPOSAL CONSIDERATIONS

Disposal methods
Waste from residues: In accordance with National, Federal, State and Local regulations.
Contaminated packaging: Empty containers should be taken to an approved waste handling site for recycling or disposal.

SECTION 14. TRANSPORT INFORMATION

International transport regulations

ADR
Not dangerous goods

RID
Not dangerous goods

DOT
Not dangerous goods

IATA
Not dangerous goods

IMDG
Not dangerous goods

SECTION 15. REGULATORY INFORMATION

EPCRA - Emergency Planning and Community Right-to-Know Act

SARA 302: No chemicals in this material are subject to the reporting requirements of SARA Title III, Section 302.

SARA 313: This material does not contain any chemical components with known CAS numbers that exceed the threshold (De Minimis) reporting levels established by SARA Title III, Section 313.

Clean Air Act
This product neither contains, nor was manufactured with a Class I or Class II ODS as defined by the U.S. Clean Air Act Section 602 (40 CFR 82, Subpt. A, App.A + B).
This product does not contain any hazardous air pollutants (HAP), as defined by the U.S. Clean Air Act Section 12 (40 CFR 61).
This product does not contain any chemicals listed under the U.S. Clean Air Act Section 112(r) for Accidental Release Prevention (40 CFR 68.130, Subpart F).
This product does not contain any chemicals listed under the U.S. Clean Air Act Section 111 SOCMI Intermediate or Final VOC's (40 CFR 60.489).

Clean Water Act
This product does not contain any Hazardous Substances listed under the U.S. CleanWater Act, Section 311, Table 116.4A.
This product does not contain any Hazardous Chemicals listed under the U.S. CleanWater Act, Section 311, Table 117.3.

Massachusetts Right To Know
No components are subject to the Massachusetts Right to Know Act.

**Pennsylvania Right To Know**

<table>
<thead>
<tr>
<th>Chemical</th>
<th>CAS Number</th>
<th>Concentration</th>
</tr>
</thead>
<tbody>
<tr>
<td>AMMONIUMSULFAAT</td>
<td>7783-20-2</td>
<td>0.1 - 1 %</td>
</tr>
<tr>
<td>DOXORUBICIN HYDROCHLORIDE</td>
<td>25316-40-9</td>
<td>0.1 - 1 %</td>
</tr>
</tbody>
</table>

**California Prop 65**

<table>
<thead>
<tr>
<th>Chemical</th>
<th>CAS Number</th>
<th>Concentration</th>
</tr>
</thead>
<tbody>
<tr>
<td>DOXORUBICIN HYDROCHLORIDE</td>
<td>25316-40-9</td>
<td></td>
</tr>
</tbody>
</table>

**WARNING!** This product contains a chemical known to the State of California to cause cancer.

**WARNING:** This product contains a chemical known to the State of California to cause birth defects or other reproductive harm.

**Other regulations**

According to Article 1, item 5 (a) of CLP Regulation (EC) 1272/2008, medicinal products in the finished state for human use, as defined in 2001/83/EC, are excepted from classification and other criteria of 1272/2008. Restricted to professional users.

This product is not subject to TSCA and TSCA 12(b) Export notification because Food, Drugs and cosmetic products are exempt.

**The components of this product are reported in the following inventories:**

**REACH**

- Not in compliance with the inventory
- CHOLESTEROL
- AMMONIUMSULFAAT
- 1,2-distearoyl-sn-glycero-3-phospho-(1’-rac-glycerol) (sodium salt)
- DOXORUBICIN HYDROCHLORIDE
- hydrogenated soybean lecithin
- This product is not subject to TSCA and TSCA 12(b) Export notification because Food, Drugs and cosmetic products are exempt.

**CH INV**

- Not in compliance with the inventory
- CHOLESTEROL
- AMMONIUMSULFAAT
- 1,2-distearoyl-sn-glycero-3-phospho-(1’-rac-glycerol) (sodium salt)

**TSCA**

- Not On TSCA Inventory
<table>
<thead>
<tr>
<th>DSL</th>
<th>This product contains the following components that are not on the Canadian DSL nor NDSL.</th>
</tr>
</thead>
<tbody>
<tr>
<td>AICS</td>
<td>Not in compliance with the inventory</td>
</tr>
<tr>
<td>NZIoC</td>
<td>Not in compliance with the inventory</td>
</tr>
<tr>
<td>ENCS</td>
<td>Not in compliance with the inventory</td>
</tr>
<tr>
<td>ISHL</td>
<td>Not in compliance with the inventory</td>
</tr>
<tr>
<td>KECI</td>
<td>Not in compliance with the inventory</td>
</tr>
<tr>
<td>PICCS</td>
<td>Not in compliance with the inventory</td>
</tr>
</tbody>
</table>
SECTION 16. OTHER INFORMATION

Further information

NFPA:

<table>
<thead>
<tr>
<th>Health</th>
<th>Flammability</th>
<th>Instability</th>
</tr>
</thead>
</table>

Special hazard.

HMIS III:

<table>
<thead>
<tr>
<th>HEALTH</th>
<th>FLAMMABILITY</th>
<th>PHYSICAL HAZARD</th>
</tr>
</thead>
</table>

0 = not significant, 1 = Slight, 2 = Moderate, 3 = High, 4 = Extreme, * = Chronic

Revision Date: 2015/04/21

Date and Number Formats

This document uses the following notation for printing dates and numbers:

Date: Dec 31th, 2012 as 2012/12/31

Numbers: 123456,78 as 12,345.67
The information provided in this Safety Data Sheet is correct to the best of our knowledge, information and belief at the date of its publication. The information given is designed only as a guidance for safe handling, use, processing, storage, transportation, disposal and release and is not to be considered a warranty or quality specification. The information relates only to the specific material designated and may not be valid for such material used in combination with any other materials or in any process, unless specified in the text.

US / EN