Material Safety Data Sheet

# KADCYLA™ Solution

## SECTION 1: Identification of the substance/mixture and of the company/undertaking

### 1.1. Product identifier

| | |
|---|---|
| Product name | KADCYLA™ Solution |
| Product code | CSE-3090 |
| Synonyms | - T-DM1 (RO5304020) 2% aqueous solution with excipients |

### 1.2. Relevant identified uses of the substance or mixture and uses advised against

| | |
|---|---|
| Use | - formulated pharmaceutical active substance (antineoplastic) |

### 1.3. Details of the supplier of the safety data sheet

Company information

Enquiries:
Hoffmann-La Roche Inc.
340 Kingsland Street
USA-Nutley, N.J. 07110-1199
United States of America

Phone 001-973/235 50 00
E-Mail info.sds@roche.com

US Emergency phone: (800)-827-6243
US Chemtrec phone: (800)-424-9300

Local representation:

### 1.4. Emergency telephone number

| | |
|---|---|
| Emergency telephone number | US emergency phone: (800)-827-6243 |

## SECTION 2: Hazards identification

### Emergency Overview

| | |
|---|---|
| Form | liquid |
| Color | colorless |
| Hazard Overview | - May cause allergic reactions.<br>- Harmful if swallowed.<br>- May cause birth defects based on information on related materials |

| | |
|---|---|
| Potential Health Effects | - Exposure: Inhalation, Ingestion, Skin contact, Eye contact<br>- Target Organs: liver, Cardiovascular system, gastrointestinal system, Hematopoietic/blood system, Immune System, respiratory system<br><br>- Acute Effects: May cause allergic reactions., Harmful if swallowed., May cause headache., May cause musculoskeletal effects., May cause general body weakness, fatigue and nausea.<br><br>- Chronic Effects: May cause hepatic (liver) system effects., Signs and symptoms may include elevation of liver enzyme levels and jaundice (yellowing of the skin and eyes)., May cause cardiovascular effects., Signs and symptoms may include increase or decrease in blood pressure, irregular heartbeat, chest pains and cardiac arrest., May cause blood system changes., May cause respiratory effects., Signs and symptoms may include difficulty in breathing, coughing, wheezing, irritation (inflammation) and respiratory arrest.<br><br>- Carcinogenicity: not listed by NTP, IARC or OSHA |

**Classification of the substance or mixture / Label elements**

| | |
|---|---|
| GHS Classification | Health Hazards:<br>3.1 oral Acute toxicity (Category 4)<br>H302 Harmful if swallowed.<br><br>Signalword: Warning<br>Label:<br> <br>Precautionary statements:<br>- P312 Call a POISON CENTER or doctor/physician if you feel unwell. |

**Other hazards**

| | |
|---|---|
| Additional Health Information | - Conditions Aggravated: Hypersensitivity to this material and other materials in its chemical class.<br>- Reproduction Toxicity: May cause birth defects. Since this material may affect the developing fetus, females planning to have a child and pregnant women should exercise caution regarding exposure.<br>- It is also advisable for nursing mothers to exercise caution regarding exposure. |
| Note | - no further information available |

## SECTION 3: Composition/information on ingredients

| | |
|---|---|
| Characterization | antibody-drug conjugate consisting of the antibody trastuzumab (the active ingredient in Herceptin) linked to a cytotoxic agent that is a derivative of maytansine (DM1) |

| Ingredients | Concentration |
|---|---|
| ado-trastuzumab emtansine<br>CAS: 1018448-65-1 | ~ 2 % |

## SECTION 4: First aid measures

### 4.1. Description of first aid measures

| | |
|---|---|
| Eye contact | - rinse immediately with tap water for 10 minutes - open eyelids forcibly |
| Skin contact | - remove immediately contaminated clothes, wash affected skin with water and soap - do not use any solvents |
| Inhalation | - remove the casualty to fresh air and keep him/her calm<br>- in the event of symptoms get medical treatment |

### 4.2. Most important symptoms and effects, both acute and delayed

| | |
|---|---|
| Note | - no information available |

### 4.3. Indication of any immediate medical attention and special treatment needed

| | |
|---|---|
| Note to physician | - treat symptomatically |

## SECTION 5: Firefighting measures

### 5.1. Extinguishing media

| | |
|---|---|
| Suitable extinguishing media | - adapt extinguishing media to surrounding fire conditions, water spray jet, dry powder, foam, carbon dioxide |
| Flash point (liquid) | not applicable |

### 5.2. Special hazards arising from the substance or mixture

| | |
|---|---|
| Specific hazards | - Does not present a fire hazard |

### 5.3. Advice for firefighters

| | |
|---|---|
| Protection of fire-fighters | - precipitate gases/vapours/mists with water spray |

## SECTION 6: Accidental release measures

### 6.1. Personal precautions, protective equipment and emergency procedures

| | |
|---|---|
| Personal precautions | - avoid exposure |

### 6.2. Environmental precautions

| | | |
|---|---|---|
| Environmental protection | - | no special environmental precautions required |

### 6.3. Methods and material for containment and cleaning up

| | | |
|---|---|---|
| Methods for cleaning up | - | wash contaminated surfaces with sodium hydroxide solution, c(NaOH)=0.5 mol/l to 1 mol/l, and rinse with water |

## SECTION 7: Handling and storage

### 7.1. Precautions for safe handling

| | | |
|---|---|---|
| Technical measures | - | avoid formation of aerosols |

### 7.2. Conditions for safe storage, including any incompatibilities

| | | |
|---|---|---|
| Storage conditions | - | below -20°C |
| Validity | - | 24 hours, 25 °C |

## SECTION 8: Exposure controls/personal protection

### 8.1. Control parameters

| | | | |
|---|---|---|---|
| Threshold value (Roche) air | - | IOEL (Internal Occupational Exposure Limit): 0.0003 mg/m3 | *1 |

### 8.2. Exposure controls

| | | |
|---|---|---|
| General protective and hygiene measures | - | instruction of employees recommended |
| Hand protection | - | protective gloves (eg made of neoprene, nitrile or butyl rubber) |
| Eye protection | - | safety glasses |

| | | |
|---|---|---|
| *1 | referring to: | ado-trastuzumab emtansine |

## SECTION 9: Physical and chemical properties

### 9.1. Information on basic physical and chemical properties

| | |
|---|---|
| Color | colorless |
| Form | liquid |

**9.2. Other information**

| | | |
|---|---|---|
| Note | - | no information available |

## SECTION 10: Stability and reactivity

**10.1. Reactivity**

| | | |
|---|---|---|
| Note | - | no information available |

**10.2. Chemical stability**

| | | | |
|---|---|---|---|
| Stability | - | do not dilute with glucose since there cause aggregation of the protein | *2 |

**10.3. Possibility of hazardous reactions**

| | | |
|---|---|---|
| Note | - | no information available |

**10.4. Conditions to avoid**

| | | |
|---|---|---|
| Conditions to avoid | - | light |
| | - | warming |

**10.5. Incompatible materials**

| | | |
|---|---|---|
| Note | - | no information available |

**10.6. Hazardous decomposition products**

| | | |
|---|---|---|
| Note | - | no information available |

*2 referring to: Herceptin Vials (2% Trastuzumab solution with excipients)

## SECTION 11: Toxicological information

**11.1. Information on toxicological effects**

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| Acute toxicity | - | HNSTD | 30 | mg/kg | (i.v., cynomolgus monkey) | | *1 |
| | - | HNSTD | 20 | mg/kg | (i.v., rat) | | *1 |
| | - | $LD_{50}$ | 0 | to 5 | mg/kg (oral, mouse) (OECD No. 423 (Acute Toxic Class Method)) | | *3 |
| Subacute toxicity | - | HNSTD | 10 | mg/kg/3w | (i.v., cynomolgus monkey, 9 weeks) | | *1 |
| Sensitization | - | anaphylactic reactions may occur following the intravenous application of proteins; rare cases of hypersensitivity have been described | | | | | *4 |

| | | |
|---|---|---|
| Note | - | HNSTD = Highest Non-Severely Toxic Dose |

| | | |
|---|---|---|
| *1 | referring to: | ado-trastuzumab emtansine |
| *3 | referring to: | Ansamitosin P3 |
| *4 | referring to: | Trastuzumab |

## SECTION 12: Ecological information

### 12.1. Toxicity

Ecotoxicity

- barely toxic for algae, growth inhibition possibly due to turbidity caused by test substance (Desmodesmus (=Scenedesmus) subspicatus)
  $ErC_{50}$ (72 h) > 100 mg/l (nominal concentration)
  $EyC_{50}$ (72 h) ~ 100 mg/l (nominal concentration)
  (OECD No. 201) *1
- barely toxic for planktonic crustaceans (Daphnia magna)
  $EC_{50}$ (48 h) > 100 mg/l (nominal concentration)
  NOEC (48 h) 100 mg/l (nominal concentration)
  (OECD No. 202) *1
- barely toxic for fish (guppy)
  $LC_{50}$ (96 h) > 100 mg/l (nominal concentration)
  NOEC (96 h) < 100 mg/l (nominal concentration)
  (OECD No. 203, semistatic) *1
- barely inhibitory on aerobic bacterial respiration (activated sludge)
  concentration (14 d) 49.5 mg/l (nominal concentration)
  (Manometric Respirometry Test, OECD No. 301 F) *1

### 12.2. Persistence and degradability

Ready biodegradability

- readily biodegradable
  84 %, 28 d
  (Manometric Respirometry Test, OECD No. 301 F) *1

### 12.3. Bioaccumulative potential

Note - no information available

### 12.4. Mobility in soil

Note - no information available

### 12.5. Results of PBT and vPvB assessment

Note - no information available

### 12.6. Other adverse effects

Note - no information available

| | | |
|---|---|---|
| *1 | referring to: | ado-trastuzumab emtansine |

## SECTION 13: Disposal considerations

**13.1. Waste treatment methods**

| | |
|---|---|
| Waste from residues | - observe local/national regulations regarding waste disposal<br>- incinerate in qualified installation with flue gas scrubbing |

## SECTION 14: Transport information

| | |
|---|---|
| Note | - not classified by transport regulations, proper shipping name non-regulated |

## SECTION 15: Regulatory information

**15.1. Safety, health and environmental regulations/legislation specific for the substance or mixture**

| | |
|---|---|
| TSCA Status | - FDA Exemption - not on inventory |
| Reporting Requirements | - The United States Environmental Protection Agency (USEPA) has not established a Reportable Quantity (RQ) for releases of this material.<br>- In New Jersey, report all releases which are likely to endanger the public health, harm the environment or cause a complaint to the NJDEPE Hotline (1-609-292-5560) and to local officials.<br>- State and local regulations vary and may impose additional reporting requirements. |

## SECTION 16: Other information

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|---|---|
| Edition documentation | - changes from previous version in sections 2, 3, 6, 8, 11, 16 |

The information in this safety data sheet is based on current scientific knowledge. It should not be taken as expressing or implying any warranty concerning product characteristics.