Safety Data Sheet

KADCYLA(R) Lyophilized Powder in Vials (160 mg)

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

1.1. Product identifier

Product name	KADCYLA(R) Lyophilized Powder in Vials (160 mg)
Product code	RO5304020-F02
Synonyms	- T-DM1 with excipients lyophilized - KADCYLA Lyophilized Vials

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

Use	-	pharmaceutical active substance (antineoplastic)	*1

1.3. Details of the supplier of the safety data sheet

Company information

Enquiries:
Genentech, Inc.
1 DNA Way
South San Francisco
USA-CA 94080
United States of America

Phone 001-(650) 225-1000
E-Mail info.sds@roche.com
US Chemtrec phone:
(800)-424-9300

Local representation:

1.4. Emergency telephone number

Emergency telephone number: US Chemtrec phone: (800)-424-9300

1 referring to: ado-trastuzumab emtansine

SECTION 2: Hazards identification

Classification of the substance or mixture / Label elements

GHS Classification

Health Hazards:

3.1 Acute toxicity (Category 4)
H312 Harmful in contact with skin.

3.1 Acute toxicity (Category 4)
H332 Harmful if inhaled.

3.1 Acute toxicity (Category 3)
H301 Toxic if swallowed.

3.5 Germ cell mutagenicity (Category 1B)
H340 May cause genetic defects.

3.7 Reproductive toxicity (Category 1B)
H360FD May damage fertility. May damage the unborn child.

Signalword: Danger

Label:

Precautionary statements:

- P201 Obtain special instructions before use.
- P280 Wear protective gloves/ protective clothing / eye protection / face protection.
- P301 + P310 IF SWALLOWED: Immediately call a POISON CENTER or doctor/physician.
- P302 + P352 IF ON SKIN: Wash with plenty of soap and water.
- P304 + P312 IF INHALED: Call a POISON CENTER or doctor/physician if you feel unwell.
- P309 + P310 IF exposed or if you feel unwell: Immediately call a POISON CENTER or doctor/physician.

Other hazards

Note

- no further information available

SECTION 3: Composition/information on ingredients

Characterization

Ado-trastuzumab emtansine with other inactive ingredients

Ingredients	Concentration	GHS-Classification (pure ingredient)
ado-trastuzumab emtansine 1018448-65-1	~ 24 %	- Combustible dust (No category), USH003 - Acute toxicity (Category 3), H311 - Acute toxicity (Category 2), H330 - Acute toxicity (Category 2), H300 - Skin corrosion/irritation (Category 2), H315 - Germ cell mutagenicity (Category 1B), H340 - Carcinogenicity (Category 2), H351 - Reproductive toxicity (Category 1B), H360FD - Specific target organ toxicity - Single exposure (Category 2), H371

For the full text of the H-phrases mentioned in this Section, see Section 16.

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 - 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	- consider dust explosion 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	-	prevent any exposure

6.2. Environmental precautions

Environmental protection	-	if the substance reaches waters or the sewer system, inform the competent authority

6.3. Methods and material for containment and cleaning up

Methods for cleaning up	-	collect solids (avoid dust formation) and hand over to waste removal
	-	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

Suitable materials	-	glass

7.2. Conditions for safe storage, including any incompatibilities

Storage conditions	-	2 - 8 °C
	-	do not freeze
	-	protected from light
Validity	-	36 months, 2 to 8 °C, see expiry date on the label

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 mandatory

Respiratory protection	- Respiratory protection is recommended as a precaution to minimize exposure. Effective engineering controls are considered to be the primary means to control worker exposure. Respiratory protection should not substitute for feasible engineering controls. - Respiratory protection is recommended for dusty operations. - respiratory protection not necessary during normal operations
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	white or practically white
Form	sterile, lyophilized powder
Solubility	soluble, water

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 - humidity

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
	- LD_{50} 0 to 50 mg/kg (dermal, rat)	*3
	- LC_0 0.5 µg/l (inhal., rat, 4 h) (OECD No. 403) LC_{100} 11.5 µg/l (inhal., rat, 4 h) (OECD No. 403)	*3
Subacute toxicity	- HNSTD 10 mg/kg/3w (i.v., cynomolgus monkey, 9 weeks)	*1
Local effects	- skin, eyes, mucous membranes: corrosive	*4
Sensitization	- anaphylactic reactions may occur following the intravenous application of proteins; rare cases of hypersensitivity have been described	*5
Mutagenicity	- negative (Ames test)	*4
	- OECD No. 474 (Micronucleus Test); positive: evidence of aneugenicity and/or clastogenicity	*4
Note	- HNSTD = Highest Non-Severely Toxic Dose	
Potential Health Effects	- Exposure: Inhalation, Ingestion, Skin contact, Eye contact - Target Organs: liver, Cardiovascular system, gastrointestinal system, Hematopoietic/blood system, Immune System, respiratory system - Acute Effects: May cause allergic reactions., Harmful if swallowed., May cause headache., May cause musculoskeletal effects., May cause general body weakness, fatigue and nausea. - 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. - Carcinogenicity: not listed by NTP, IARC or OSHA	

Additional Health Information	-	Conditions Aggravated: Hypersensitivity to this material and other materials in its chemical class.

1	referring to:	ado-trastuzumab emtansine
3	referring to:	Ansamitocin P3
4	referring to:	DM1
5	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
- incinerate in qualified installation with flue gas scrubbing

SECTION 14: Transport information

IATA	Class	UN/ID	PG		PI	Label	Mark
	6.1	3249	III		670/677	6.1	

IMDG	Class	UN	PG	EmS	PI	Label	Mark
	6.1	3249	III	F-A S-A	P002/ -	6.1	

RID/ADR	Class	UN	PG	Haz.no	PI	Label	Mark	Classif. code
	6.1	3249	III	60	P002/ -	6.1		T2

DOT	Class	UN/ID	PG	PI	RQ	Label	Haz.no
	6.1	3249	III			6.1	

Proper shipping name MEDICINE, SOLID, TOXIC, N.O.S.

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. - 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. - State and local regulations vary and may impose additional reporting requirements.

SECTION 16: Other information

Full text of H-Statements referred to under section 3

H300	Fatal if swallowed.
H311	Toxic in contact with skin.
H315	Causes skin irritation.
H330	Fatal if inhaled.
H340	May cause genetic defects.
H351	Suspected of causing cancer.
H360FD	May damage fertility. May damage the unborn child.
H371	May cause damage to organs.
USH003	May form combustible dust concentrations in the air

Note	- This product may be shipped using De Minimis Quantity Exceptions, if the requirements of US 49 CFR §173.4b and ICAO 5.6/IATA 2.6.10 are met. - Please note this Safety Data Sheet for the bulk product does not apply for the finished, packaged medicinal product intended for the final user.
Edition documentation	- changes from previous version in sections 2, 3, 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.