Safety Data Sheet for Drug product

Date of issue: 08-JUL-2014
Replaces version of: 08-JUL-2014
ZORTRESS TA 0.75MG 60 025-10-07-0 (US02)

1. Identification of the substance/preparation and of the company

Product name	ZORTRESS TA 0.75MG 60
Chemical Class	Rapamycin derivative
Generic Name	Rapamycin, 42-O-(2-hydroxyethyl)-
Pharmacological Action	immunosuppressant
Usage	Drug product (pharmaceutical bulk, primary packed, finished product, pharmaceutical intermediate)
Company name	Novartis Pharmaceuticals Corporation One Health Plaza East Hanover, NJ 07936-1080 USA
Emergency phone number	+1 862 778 7777

2. Hazards identification

For side effects, which could also have impact for people working with this substance, please refer to the Patient Information Leaflet.

3. Composition / information on ingredients

For classification of declared components, see section 15, "Regulatory Information"

Chemical Name	Contains:	CAS Number
Rapamycin, 42-O-(2-hydroxyethyl)-	0.1 - 2 %	159351-69-6

Remaining components are inert ingredients.

For TLV values of declared components, see Section 8, Exposure controls / Personal

4. First aid measures

Eye Contact	Immediately rinse eyes thoroughly with running water as long as possible (approx. 15 min). Take injured quickly to factory medical center or call an ambulance (code word: eye accident).
Skin Contact	Remove contaminated clothing. Rinse contaminated skin immediately with plenty of water and soap and seek medical advice.
Inhalation	Remove the victim from danger zone, avoid further exposure.
Ingestion	If swallowed, seek medical advice immediately and show this container or label.
Notes to Physician	General measures to eliminate the substance and to reduce absorption.

5. Fire fighting measures

Suitable Extinguishing Media	Water spray or fog, foam, dry chemical powder, CO2, dry sand
Unsuitable Extinguishing Media	No restrictions
Dangerous Combustion Products	carbon oxides, nitrogen oxides
Protective equipment for firefighters	Wear self-contained breathing apparatus and fire protective suite.

6. Accidental release measures

Personal precautions	Avoid contact with skin, eyes and clothing.
Environmental	Must not be released into sewers, drains or wells.

precautions

Methods for cleaning Transfer large quantities into a container. Clean up the rest with absorbent material and discharge properly.

7. Handling and storage

No special handling requirements for normal use of this material.
Store in a dry and cool place and observe special instructions from supplier.

8. Exposure controls / Personal protection

Occupational Exposure Limit (OEL)

no data available

TLV values of declared components
Contains:
Rapamycin, 42-O-(2-hydroxyethyl)-

List type	mg/m3	
Internal exposure limit	0.02	/ /

Personal protection for open handling

Health care personnel		Safety glasses (EN166) Lab coat Disposable gloves (EN374)

9. Physical and chemical properties

Formulation Tablet
Flash Point not available

10. Stability and reactivity

Under the normal conditions of use, the product is stable.

11. Toxicological information

Acute Toxicity

Data of Rapamycin, 42-O-(2-hydroxyethyl)-
LD50 oral: > 2000 mg/kg
Species: mouse

Data of Rapamycin, 42-O-(2-hydroxyethyl)-
LD50 oral: > 2000 mg/kg
Species: rat
Method: 96/54/EC, B.1 tris (ATC Method)

Irritation, Corrosion

Values of Rapamycin, 42-O-(2-hydroxyethyl)-
Eye irritation not tested.

Data of Rapamycin, 42-O-(2-hydroxyethyl)-
Skin (Species: rabbit) non irritant
Method: 92/69/EC (L383) B.4 * Acute toxicity (skin irritation)

Sensitisation

Data of Rapamycin, 42-O-(2-hydroxyethyl)-
Skin (Species: guinea pig) not sensitizing
Method: 92/69/EEC B.6 Modified Maximization Test

Mutagenicity

Values of Rapamycin, 42-O-(2-hydroxyethyl)-
The product showed negative results in in vitro mutagenicity studies. The product showed negative results in in vivo mutagenicity studies.

Data of Rapamycin, 42-O-(2-hydroxyethyl)-

	Negative (Micronucleus Test) oral, Species: mouse, Cell: Bone marrow
	Data of Rapamycin, 42-O-(2-hydroxyethyl)- Negative (AMES-Test (reverse mutation assay)) in vitroCell: Strains of Salmonella typhimurium and Escherichia coli.
Chronic Effects	Values of Rapamycin, 42-O-(2-hydroxyethyl)- This substance causes concern for man owing to possible secondary carcinogenic effects due to immunosuppression. Immunosuppressants are known to produce cancer in transplant patients. Immunosuppression works in a dose-response relationship. The development of cancers is linked to the level of immunosuppression needed for transplantation. Below these levels, with the immune system functioning uninhibited, cancer will not develop due to exposure to immunosuppressants at work. Handling this substance, precautionary measures should be taken according to workplace health risk assessment.
	Data of Rapamycin, 42-O-(2-hydroxyethyl)- Moderate Toxicity (Repeated Dose Toxicity (subchronic study)) NTEL oral: 0.15 mg/kg/d Species: mouse, Organ: Multiple organs Dosage: 15 mg/kg/d, Duration: 13 weeks
	Data of Rapamycin, 42-O-(2-hydroxyethyl)- Moderate Toxicity (Repeated Dose Toxicity (subchronic study)) NTEL oral: 0.1 mg/kg/d Species: monkey, Organ: Multiple organs Duration: 52 weeks
Reproduction Toxicity	Values of Rapamycin, 42-O-(2-hydroxyethyl)- There is no evidence for reproductive toxicity.

12. Ecological information

Biological Elimination	Data of Rapamycin, 42-O-(2-hydroxyethyl)- Degradation: 2 % (aerobic: Temperature: 21.7 - 22.4 °C BOD/ThODX100) Not readily degradable Initial conc.: 100 mg/l, Duration: 28 days Method: 92/69/EC (L383) C.4-D * Manometric respirometry Inhibitory effects can be excluded.
Fish acute toxicity	Data of Rapamycin, 42-O-(2-hydroxyethyl)- LC50: > 18.4 mg/l Species: common carp (cyprinus carpio) Exp. time: 96 hours Method: EEC directive 92/69, Part C.1. Maximum testing concentration due to the substance's water solubility limit.
Fish chronic toxicity	Data of Rapamycin, 42-O-(2-hydroxyethyl)- LOEC: 0.0083 mg/l NOEC: NOEC: 0.0021 mg/l Species: zebra fish (danio rerio) Exp. time: 35 days Method: OECD 210 * 1992
Aquatic invertebrate acute toxicity	Data of Rapamycin, 42-O-(2-hydroxyethyl)- EC50: > 8 mg/l Species: daphnia magna (water flea) Exp. time: 48 hours Method: 92/69/EEC (L383) C.2 * Acute toxicity for daphnia Maximum testing concentration due to the substance's water solubility limit.
Aquatic invertebrate chronic toxicity	Data of Rapamycin, 42-O-(2-hydroxyethyl)- LOEC: 0.000029 mg/l NOEC: NOEC: 0.000014 mg/l Species: daphnia magna (water flea) Exp. time: 21 days Method: OECD 211 * 2008

Algae Toxicity	Data of Rapamycin, 42-O-(2-hydroxyethyl)- EC50: > 16 mg/l NOEC: 7 mg/l Species: Pseudokirchneriella subcapitata/Selenastrum capricornutum (Green algae) Exp. time: 96 hours Method: 92/69/EC (L383) C.3 Maximum testing concentration due to the substance's water solubility limit.
Bacterial Respiration Inhibition	Data of Rapamycin, 42-O-(2-hydroxyethyl)- IC20: > 1000 mg/l IC50: > 1000 mg/l Species: activated sludge Exp. time: 3 hours Method: Inhibition of Oxygen Consumption by activated sludge (87/302/EEC), Part C

13. Disposal considerations

Disposal Requirements Fill into suitable waste receptacles, seal and label them properly. Incineration in an approved, controlled furnace with combustion gas scrubbing and emission gas control. Local regulations should be adhered to.

14. Transport information

Regulation	Class	UN No.	PG	Label	LQ
RID/ADR:	not restricted	0			N.A.
IMDG-Code:	not restricted	0			
ICAO/IATA-DGR:	not restricted	0			

ICAO/IATA-DGR: no dangerous good
Proper shipping name: -

15. Regulatory information

Classifications of components:

Chemical Name	Contains:	CAS Number	Picto	Signal Word	Classification
Rapamycin, 42-O-(2-hydroxyethyl)-	0.1 - 2 %	159351-69-6		D	H351, H372, H410

Remaining components are inert ingredients.

16. Other information

Changes since the previous version in Section
1. Identification of the substance/preparation and of the company
4. First aid measures
8. Exposure controls / Personal protection

Abbreviations used

H351: Suspected of causing cancer.
H372: Causes damage to organs through prolonged or repeated exposure.
H410: Very toxic to aquatic life with long lasting effects.

Recipient
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Product should be stored, handled and used in accordance with good industrial hygiene practices and in conformity with

legal regulations. The information contained herein is based on the present state of our knowledge and is intended to describe our products from the point of view of safety requirements. It should therefore not be construed as guaranteeing specific properties.