

Safety Data Sheet

ERIVEDGE(R) Capsules (150 mg)

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

1.1. Product identifier

Product name	ERIVEDGE(R) Capsules (150 mg)	
Product code	SAP-10130925	
Synonyms	- Hedgehog signaling pathway antagonist RO5450815	*1

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

1.4. Emergency telephone number

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

*1 referring to: Vismodegib

ERIVEDGE(R) Capsules (150 mg)

SECTION 2: Hazards identification

Classification of the substance or mixture / Label elements

GHS Classification

Health Hazards:

- 3.7 Reproductive toxicity (Category 1B)
H360D May damage the unborn child.
- 3.7 Reproductive toxicity (Category 1B)
H360F May damage fertility.
- 3.9 Specific target organ toxicity - Repeated exposure (Category 2)
H373 May cause damage to organs through prolonged or repeated exposure.

Signalword: Danger

Label:



Precautionary statements:

- P201 Obtain special instructions before use.
- P260 Do not breathe dust
- P308 + P313 IF exposed or concerned: Get medical advice/attention.
- P273 Avoid release to the environment.
- P501 Dispose of contents/container to waste disposal as hazardous waste

Other hazards

Note - no information available

SECTION 3: Composition/information on ingredients

Characterization

mixture of approx. 35% Vismodegib with excipients

Ingredients

Concentration

GHS-Classification
(pure ingredient)

Vismodegib
879085-55-9

35.3 %

- Reproductive toxicity (Category 1B), H360D
- Reproductive toxicity (Category 1B), H360F
- Specific target organ toxicity - Repeated exposure (Category 2), H373

Microcrystalline cellulose
9004-34-6

20.5 %

Lactose monohydrate
64044-51-5

16.8 %

Sodium starch glycolate
9063-38-1

4.1 %

ERIVEDGE(R) Capsules (150 mg)

Povidone K29/32 9003-39-8	2.5 %	
Sodium lauryl sulfate 151-21-3	1.6 %	<ul style="list-style-type: none">- Flammable solids (Category 2), H228- Acute toxicity (Category 4), H332- Acute toxicity (Category 4), H302- Skin corrosion/irritation (Category 2), H315- Serious eye damage/eye irritation (Category 1), H318- Specific target organ toxicity - Single exposure (Category 3), H335
Talc 14807-96-6		

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

*1 referring to: Vismodegib

SECTION 4: First aid measures

4.1. Description of first aid measures

Eye contact	<ul style="list-style-type: none">- rinse immediately with tap water for 10 minutes - open eyelids forcibly
Skin contact	<ul style="list-style-type: none">- remove immediately contaminated clothes, wash affected skin with water and soap - do not use any solvents
Inhalation	<ul style="list-style-type: none">- 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
- after accidental exposure women should get medical advice from a physician
- preserve blood and urine samples

SECTION 5: Firefighting measures

5.1. Extinguishing media

Suitable extinguishing media	<ul style="list-style-type: none">- water spray jet, dry powder, foam, carbon dioxide- adapt extinguishing media to surrounding fire conditions
Flash point (liquid)	not applicable

ERIVEDGE(R) Capsules (150 mg)

5.2. Special hazards arising from the substance or mixture

- Specific hazards
- formation of toxic combustion gases (nitrogen oxides, hydrogen chloride, sulfur oxides) possible
 - consider dust explosion hazard
 - substance is hazardous for water: contain fire-fighting wastewater

5.3. Advice for firefighters

- Protection of fire-fighters
- precipitate gases/vapours/mists with water spray
 - do not inhale explosion and/or combustion gases
 - use self-contained breathing apparatus

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
- do not allow to enter drains or waterways
 - the solvent should be held back due to 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

SECTION 7: Handling and storage

7.1. Precautions for safe handling

- Technical measures
- processing in closed systems, if possible superposed by inert gas (e.g. nitrogen)
 - avoid dust formation
 - connect the equipment to earth, avoid effective sources of ignition

7.2. Conditions for safe storage, including any incompatibilities

- Storage conditions
- 15 - 30 °C
 - protected from light and humidity
- Validity
- 24 months, 15 to 30 °C
- Packaging materials
- drums
 - lined with polyethylene bag

ERIVEDGE(R) Capsules (150 mg)

- high density polyethylene (HDPE) bottles with a child-resistant polypropylene screw cap

SECTION 8: Exposure controls/personal protection

8.1. Control parameters

Threshold value (USA) air	- OSHA-PEL: 5 mg/m ³ (respirable dust fraction)	*2
	- OSHA-PEL: 15 mg/m ³ (total dust)	*2
	- NIOSH-REL: 5 mg/m ³ (respirable dust fraction)	*2
	- NIOSH-REL: 10 mg/m ³ (total dust)	*2
	- ACGIH-TLV: 2 mg/m ³ (not classifiable as a human carcinogen, respirable fraction)	*3
	- OSHA-PEL: 2 mg/m ³ (respirable fraction)	*3
	- NIOSH-REL: 2 mg/m ³ (respirable fraction)	*3
	- OSHA-PEL: 5 mg/m ³ (respirable fraction)	*4
	- OSHA-PEL: 15 mg/m ³ (total dust)	*4
	- ACGIH-TLV: 10 mg/m ³	*5
	- OSHA-PEL: 5 mg/m ³ (respirable fraction)	*5
	- OSHA-PEL: 15 mg/m ³ (total dust)	*5
	- NIOSH-REL: 5 mg/m ³ (respirable fraction)	*5
	- NIOSH-REL: 10 mg/m ³ (total dust)	*5
	Threshold value (Roche) air	- IOEL (Internal Occupational Exposure Limit): 300 ng/m ³

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. - in case of open handling or accidental release: particle mask or respirator with independent air supply
Hand protection	- protective gloves (eg made of neoprene, nitrile or butyl rubber)
Eye protection	- safety glasses
*1 referring to:	Vismodegib
*2 referring to:	Microcrystalline cellulose
*3 referring to:	Talc
*4 referring to:	Lactose
*5 referring to:	Sodium starch glycolate

SECTION 9: Physical and chemical properties

9.1. Information on basic physical and chemical properties

Color	grey pink
-------	--------------

ERIVEDGE(R) Capsules (150 mg)

Form	capsules	
Solubility	0.879 mg/l, water (20 °C, pH 6.8, OECD No. 105)	*1
Partition coefficient	log P _{ow} 1.59 (HPLC Method, OECD No. 117)	*1
Melting temperature	186 to 188 °C (OECD No. 102)	*1

9.2. Other information

Note - no information available

*1 referring to: Vismodegib

SECTION 10: Stability and reactivity

10.1. Reactivity

Note - no information available

10.2. Chemical stability

Note - no information available

10.3. Possibility of hazardous reactions

Note - no information available

10.4. Conditions to avoid

Conditions to avoid - above 300 °C violent decomposition with a strong performance of decomposition *1

10.5. Incompatible materials

Note - no information available

10.6. Hazardous decomposition products

Note - no information available

*1 referring to: Vismodegib

ERIVEDGE(R) Capsules (150 mg)

SECTION 11: Toxicological information

11.1. Information on toxicological effects

Acute toxicity	- LD ₅₀ > 2'000 mg/kg (oral, rat) (OECD No. 423 (Acute Toxic Class Method))	*1
	- LD ₅₀ > 2'000 mg/kg (oral, rat)	*6
Subacute toxicity	- NOAEL 50 mg/kg/d (oral, dog, 4 weeks); female	*1
Local effects	- skin: non-irritant (rat; OECD No. 404)	*1
Subchronic toxicity	- NOAEL 50 mg/kg (oral, mouse; 84 d); males; not established for females based on the effects on female reproductive organs	*1
	- Doses \geq 50 mg/kg resulted in decreased uterine weight (females). Doses \geq 100 mg/kg resulted in malocclusion and missing teeth, slight decrease in body weight gain, decreased ovarian weight (females) and hair follicle atrophy.	*1
Chronic toxicity	- NOAEL < 5 mg/kg/d (oral, rat; 26 weeks)	*1
Mutagenicity	- not mutagenic (various in vivo and in vitro test systems)	*7
	- not mutagenic (various in vivo and in vitro test systems)	*1
Reproductive toxicity	- teratogenic and embryotoxic (oral, rat); LOEL = 10 mg/kg/d	*1
Potential Health Effects	- Exposure: Inhalation, Ingestion, Skin contact, Eye contact - Target Organs: gastrointestinal system, Skeletal system - Acute Effects: May cause gastrointestinal effects., Signs and symptoms may include nausea, vomiting, diarrhea, constipation, cramps, and loss of appetite., May cause musculoskeletal effects., Signs and symptoms may include muscle weakness or pain and skeletal abnormalities., May cause loss of hair., May cause general body weakness, fatigue and nausea. - Chronic Effects: No adverse effects known - Carcinogenicity: not listed by NTP, IARC or OSHA - Carcinogenicity: IARC Gr3 not classifiable	*8

*1 referring to:	Vismodegib
*6 referring to:	Magnesium stearate
*7 referring to:	Sodium lauryl sulfate
*8 referring to:	Povidone K29/32

ERIVEDGE(R) Capsules (150 mg)

SECTION 12: Ecological information

12.1. Toxicity

Ecotoxicity	<ul style="list-style-type: none">- highly toxic for algae (<i>Desmodesmus</i> (=Scenedesmus) <i>subspicatus</i>) ErC₅₀ (72 h) 0.95 mg/l (nominal concentration) EyC₅₀ (72 h) 0.52 mg/l (nominal concentration) NOEC (72 h) 0.32 mg/l (nominal concentration) (OECD No. 201) *1- highly toxic for algae (<i>Pseudokirchneriella subcapitata</i>) ErC₅₀ (72 h) 0.118 mg/l EyC₅₀ (72 h) 0.099 mg/l NOEC (72 h) 0.069 mg/l (nominal concentration) (OECD No. 201) *1- barely toxic for planktonic crustaceans (nominal concentration = 100 mg/l) (<i>Daphnia magna</i>) EC₅₀ (48 h) > 100 mg/l (nominal concentration) NOEC (48 h) 0.85 mg/l (average measured concentration) (OECD No. 202) *1- <i>Daphnia magna</i> NOEC (21 d) 1.5 mg/l (nominal concentration) LOEC (21 d) > 1.5 mg/l (nominal concentration) (OECD No. 211 (semi-static)) *1- water soluble part barely toxic for fish, test performed with water accommodated fractions (zebrafish) LC₅₀ (96 h) > 1.5 mg/l (saturation concentration) NOEC (96 h) 1.5 mg/l (OECD No. 203) *1- no adverse influence on substrate biodegradation (activated sludge) concentration (14 d) 54 mg/l (nominal concentration) *1
-------------	--

12.2. Persistence and degradability

Ready biodegradability	<ul style="list-style-type: none">- not readily biodegradable 0 % BOD/ThOD, 28 d (Manometric Respirometry Test, OECD No. 301 F) *1
------------------------	--

12.3. Bioaccumulative potential

Note	<ul style="list-style-type: none">- no information available
------	--

12.4. Mobility in soil

Mobility	<ul style="list-style-type: none">- strong adsorption, low mobility (, 48 h, 20 °C) K_{oc} = 2129 to 5001 l/kg (soil) K_{oc} = 684 to 895 l/kg (activated sludge) (OECD No. 106 Adsorption/Desorption) *1
----------	---

12.5. Results of PBT and vPvB assessment

Note	<ul style="list-style-type: none">- no information available
------	--

ERIVEDGE(R) Capsules (150 mg)

12.6. Other adverse effects

Note - no information available

*1 referring to: Vismodegib

SECTION 13: Disposal considerations

13.1. Waste treatment methods

Waste from residues

- observe local/national regulations regarding waste disposal
- medicines should not be disposed of via wastewater
- return to supplier or hand over to authorized disposal company
- DO NOT FLUSH unused medications or POUR them down a sink or drain. If available in your area, use takeback programs run by household hazardous waste collection programs or community pharmacies to dispose of unused and expired medicines. If you don't have access to a takeback program, dispose of these medicines in the household trash by removing them from their original containers and mixing them with an undesirable substance, such as used coffee grounds or kitty litter.

SECTION 14: Transport information

IATA	Class	UN/ID	PG		PI	Label	Mark
	9	3077	III		956/956	9	EHS

IMDG	Class	UN	PG	EmS	PI	Label	Mark
	9	3077	III	F-A S-F	P002/IBC08	9	marine pollutant

RID/ADR	Class	UN	PG	Haz.no	PI	Label	Mark	Classif. code
	9	3077	III	90	P002/IBC08	9	EHS	M7

DOT	Class	UN/ID	PG	PI	RQ	Label	Haz.no
	9	3077	III			9	

DOT Remark: - NON-REGULATED IN NON-BULK PACKAGINGS TRANSPORTED BY MOTOR VEHICLES, RAIL CARS OR AIRCRAFT (49CFR 171.4(c)).

ERIVEDGE(R) Capsules (150 mg)

Proper shipping name ENVIRONMENTALLY HAZARDOUS SUBSTANCE, SOLID, N.O.S.

Technical name Vismodegib

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

- H228 Flammable solid.
- H302 Harmful if swallowed.
- H315 Causes skin irritation.
- H318 Causes serious eye damage.
- H332 Harmful if inhaled.
- H335 May cause respiratory irritation.
- H360D May damage the unborn child.
- H360F May damage fertility.
- H373 May cause damage to organs through prolonged or repeated exposure.

Note - 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 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.