

**1. Product and Company Identification**

Product name	ERIVEDGE™ Capsules (150 mg)	
Product code	SAP-10130925	
Use	- pharmaceutical active substance (antineoplastic)	*1
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	
Synonyms	- Hedgehog signaling pathway antagonist RO5450815	*1
*1 referring to:	Vismodegib	

2. Hazard identification**Emergency Overview**

Form	capsules
Color	grey pink
Hazard Overview	- May cause birth defects based on animal data. - may cause reproductive system effects based on animal data

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Potential Health Effects

- Exposure: Inhalation, Ingestion, Skin contact, Eye contact
- Target Organs: gastrointestinal system, Skeletal system
- Acute Effects: This material has not been tested as a whole; therefore, the information described below is based on one or more of its ingredients., 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 *2

GHS Classification

Health Hazards:

- 3.1 oral Acute toxicity (Category 5)
H303 May be harmful if swallowed.
- 3.7 D Reproductive toxicity (Category 1B)
H360D May damage the unborn child.
- 3.7 F Reproductive toxicity (Category 1B)
H360F May damage fertility.
- 3.9 Specific target organ toxicity - Repeated exposure (Category 2)
H373 May cause damage to organs.

Environmental Hazards:

- 4.1 Acute Hazardous to the aquatic environment (Category 1)
H400 Very toxic to aquatic life.
- 4.1 Chron Hazardous to the aquatic environment (Category 1)
H410 Very toxic to aquatic life with long lasting effects.

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

Additional Health Information

- Reproductive Toxicity: May cause birth defects based on animal data. May affect fertility (including sperm production, ovulation, motility and impotence) based on animal data.

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- Since this material may affect reproductive capabilities and the developing fetus, females and males planning to have a child, pregnant women and nursing mothers should exercise caution regarding potential exposure.

*2 referring to: Povidone K29/32

3. Composition/Information on ingredients

Characterization mixture of approx. 43% Vismodegib with excipients

Ingredients	Concentration
Vismodegib CAS: 879085-55-9	43 %
Microcrystalline cellulose CAS: 9004-34-6	25 %
Lactose monohydrate CAS: 64044-51-5	20.5 %
Sodium starch glycolate CAS: 9063-38-1	5 %
Povidone K29/32 CAS: 9003-39-8	3 %
Sodium lauryl sulfate CAS: 151-21-3	2 %
Talc CAS: 14807-96-6	1 %

*1 referring to: Vismodegib

4. 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
Note to physician	- treat symptomatically - after accidental exposure women should get medical advice from a physician - preserve blood and urine samples

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5. Fire-fighting measures

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
Specific hazards	<ul style="list-style-type: none">- 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
Protection of fire-fighters	<ul style="list-style-type: none">- precipitate gases/vapours/mists with water spray- do not inhale explosion and/or combustion gases- use self-contained breathing apparatus

6. Accidental release measures

Environmental protection	<ul style="list-style-type: none">- 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
Methods for cleaning up	<ul style="list-style-type: none">- collect solids (avoid dust formation) and hand over to waste removal

7. Handling and storage

Handling

Technical measures	<ul style="list-style-type: none">- 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
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Storage

Storage conditions	<ul style="list-style-type: none">- 15 - 30 °C- protected from light and humidity
Validity	<ul style="list-style-type: none">- 24 months, 15 to 30 °C
Packaging materials	<ul style="list-style-type: none">- high density polyethylene (HDPE) bottles with a child-resistant polypropylene screw cap

8. Exposure controls/Personal protection

Engineering Measures	<ul style="list-style-type: none">- see 7.
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Monitoring

Threshold value (USA) air	<ul style="list-style-type: none"> - OSHA-PEL: 5 mg/m³ (respirable dust fraction) *3 - OSHA-PEL: 15 mg/m³ (total dust) *3 - NIOSH-REL: 5 mg/m³ (respirable dust fraction) *3 - NIOSH-REL: 10 mg/m³ (total dust) *3 - ACGIH-TLV: 2 mg/m³ (not classifiable as a human carcinogen, respirable fraction) *4 - OSHA-PEL: 2 mg/m³ (respirable fraction) *4 - NIOSH-REL: 2 mg/m³ (respirable fraction) *4 - OSHA-PEL: 5 mg/m³ (respirable fraction) *5 - OSHA-PEL: 15 mg/m³ (total dust) *5 - ACGIH-TLV: 10 mg/m³ *6 - OSHA-PEL: 5 mg/m³ (respirable fraction) *6 - OSHA-PEL: 15 mg/m³ (total dust) *6 - NIOSH-REL: 5 mg/m³ (respirable fraction) *6 - NIOSH-REL: 10 mg/m³ (total dust) *6
Threshold value (Roche) air	<ul style="list-style-type: none"> - IOEL (Internal Occupational Exposure Limit): 0.001 mg/m³ *1

Personal protective equipment

Respiratory protection	<ul style="list-style-type: none"> - 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	<ul style="list-style-type: none"> - protective gloves (eg made of neoprene, nitrile or butyl rubber)
Eye protection	<ul style="list-style-type: none"> - safety glasses
General protective and hygiene measures	<ul style="list-style-type: none"> - instruction of employees mandatory

*1 referring to:	Vismodegib
*3 referring to:	Microcrystalline cellulose
*4 referring to:	Talc
*5 referring to:	Lactose monohydrate
*6 referring to:	Sodium starch glycolate

9. Physical and chemical properties

Color	grey pink	
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

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Melting temperature	186 to 188 °C (OECD No. 102)	*1
*1 referring to:	Vismodegib	
10. Stability and reactivity		
Conditions to avoid	- above 300 °C violent decomposition with a strong performance of decomposition	*1
*1 referring to:	Vismodegib	
11. Toxicological information		
Acute toxicity	- LD ₅₀ > 2'000 mg/kg (oral, rat) (OECD No. 423 (Acute Toxic Class Method))	*1
	- LD ₅₀ 1'427 mg/kg (oral, rat)	*7
	- LD ₅₀ > 2'000 mg/kg (oral, rat)	*8
Subacute toxicity	- NOAEL 50 mg/kg/d (oral, dog, 4 weeks); female	*1
Local effects	- skin: non-irritant (rat; OECD No. 404)	*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
*1 referring to:	Vismodegib	
*7 referring to:	Sodium lauryl sulfate	
*8 referring to:	Magnesium stearate	
12. Ecological information		
Ready biodegradability	- not readily biodegradable 0 % BOD/ThOD, 28 d (Manometric Respirometry Test, OECD No. 301 F)	*1
Ecotoxicity	- highly toxic for algae (<i>Desmodesmus (=Scenedesmus) subspicatus</i>) ErC ₅₀ (72 h) 0.95 mg/l (nominal concentration) EyC ₅₀ (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>) ErC ₅₀ (72 h) 0.118 mg/l EyC ₅₀ (72 h) 0.099 mg/l NOEC (72 h) 0.069 mg/l (nominal concentration) (OECD No. 201)	*1

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	<ul style="list-style-type: none">- barely toxic for planktonic crustaceans (nominal concentration = 100 mg/l) (Daphnia magna) EC₅₀ (48 h) > 100 mg/l (nominal concentration) NOEC (48 h) 0.85 mg/l (average measured concentration) (OECD No. 202) *1- Daphnia magna 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
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
*1 referring to:	Vismodegib
13. Disposal considerations	
Waste from residues	<ul style="list-style-type: none">- observe local/national regulations regarding waste disposal- incinerate in qualified installation with flue gas scrubbing- 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.
14. Transport information	
Note	<ul style="list-style-type: none">- not classified by transport regulations, proper shipping name non-regulated- provisional transport classification (under clarification)
15. Regulatory information	
TSCA Status	<ul style="list-style-type: none">- FDA Exemption - not on inventory

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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.

16. Other information

Edition documentation

- changes from previous version in sections 2, 14, 16

*1 referring to:

Vismodegib

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.