1. Product and Company Identification

Product name: ERIVEDGE(R) Capsules (150 mg)
Product code: SAP-10132195
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
**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

**GHS Classification Health Hazards:**
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.

**Signal word:** Danger

**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.
- 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
## ERIVEDGE(R) Capsules (150 mg)

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

*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

### 5. Fire-fighting measures

- **Suitable extinguishing media**
  - water spray jet, dry powder, foam, carbon dioxide
  - adapt extinguishing media to surrounding fire conditions

- **Flash point (liquid)**
  - not applicable

- **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

- **Protection of fire-fighters**
  - 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 | - 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  | - collect solids (avoid dust formation) and hand over to waste removal  

7. Handling and storage

<table>
<thead>
<tr>
<th>Handling</th>
</tr>
</thead>
</table>
| 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  

<table>
<thead>
<tr>
<th>Storage</th>
</tr>
</thead>
</table>
| Storage conditions | - 15 - 30 °C  
|                   | - protected from light and humidity  
| Validity | - 24 months, 15 to 30 °C  
| Packaging materials | - drums  
|                   | - lined with polyethylene bag  

8. Exposure controls/Personal protection

| Engineering Measures | - see 7.  

| Monitoring |
| Threshold value (USA) air | - OSHA-PEL: 5 mg/m³ (respirable dust fraction)  
|                           | - OSHA-PEL: 15 mg/m³ (total dust)  
|                           | - NIOSH-REL: 5 mg/m³ (respirable dust fraction)  
|                           | - NIOSH-REL: 10 mg/m³ (total dust)  
|                           | - ACGIH-TLV: 2 mg/m³ (not classifiable as a human carcinogen, respirable fraction)  
|                           | - OSHA-PEL: 2 mg/m³ (respirable fraction)  
|                           | - NIOSH-REL: 2 mg/m³ (respirable fraction)  
|                           | - OSHA-PEL: 5 mg/m³ (respirable fraction)  
|                           | - OSHA-PEL: 15 mg/m³ (total dust)  
|                           | - ACGIH-TLV: 10 mg/m³  
|                           | - OSHA-PEL: 5 mg/m³ (respirable fraction)  
|                           | - OSHA-PEL: 15 mg/m³ (total dust)  
|                           | - NIOSH-REL: 5 mg/m³ (respirable fraction)  
|                           | - NIOSH-REL: 10 mg/m³ (total dust)  
| Threshold value (Roche) air | - IOEL (Internal Occupational Exposure Limit): 300 ng/m³  

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Date: 20.7.12/LS (SEISMO)  
Replacing edition of: --  
Page: 4/8
ERIVEDGE(R) Capsules (150 mg)

Personal protective equipment

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

General protective and hygiene measures - 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

Melting temperature 186 to 188 °C (OECD No. 102) *1

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 - LD₅₀ > 2'000 mg/kg (oral, rat) (OECD No. 423 (Acute Toxic Class Method)) *1
- LD₅₀ 1'427 mg/kg (oral, rat) *7
- LD₅₀ > 2'000 mg/kg (oral, rat) *8

Subacute toxicity - NOAEL 50 mg/kg/d (oral, dog, 4 weeks); female *1
ERIVEDGE(R) Capsules (150 mg)

Local effects  
- skin: non-irritant (rat; OECD No. 404)  

Chronic toxicity  
- NOAEL < 5 mg/kg/d (oral, rat; 26 weeks)  

Mutagenicity  
- not mutagenic (various in vivo and in vitro test systems)  

Reproductive toxicity  
- teratogenic and embryotoxic (oral, rat); LOEL = 10 mg/kg/d  

*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)  

Ecotoxicity  
- highly toxic for algae (Desmodesmus (=Scenedesmus) subspicatus)  
  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)  

- highly toxic for algae (Pseudokirchneriella subcapitata)  
  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)  

- 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)  

- 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))  

- 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)  

- no adverse influence on substrate biodegradation (activated sludge)  
  concentration (14 d) 54 mg/l (nominal concentration)  

Mobility  
- strong adsorption, low mobility (. 48 h, 20 °C)  
  KOC = 2129 to 5001 l/kg (soil)  
  KOC = 684 to 895 l/kg (activated sludge)  
  (OECD No. 106 Adsorption/Desorption)  

*1 referring to: Vismodegib
13. Disposal considerations

Waste from residues
- 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

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<td>III</td>
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</tr>
</tbody>
</table>

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

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

Technical name Vismodegib

15. Regulatory information

TSCA Status
- FDA Exemption - not on inventory
**ERIVEDGE(R) Capsules (150 mg)**

<table>
<thead>
<tr>
<th>Reporting Requirements</th>
</tr>
</thead>
<tbody>
<tr>
<td>- The United States Environmental Protection Agency (USEPA) has not established a Reportable Quantity (RQ) for releases of this material.</td>
</tr>
<tr>
<td>- 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.</td>
</tr>
<tr>
<td>- State and local regulations vary and may impose additional reporting requirements.</td>
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</table>

**16. Other information**

<table>
<thead>
<tr>
<th>Edition documentation</th>
</tr>
</thead>
<tbody>
<tr>
<td>- first edition</td>
</tr>
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*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.