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

1.1. Product identifier

<table>
<thead>
<tr>
<th>Product name</th>
<th>ACTIVASE® Vials (50 mg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Product code</td>
<td>SAP-10053299</td>
</tr>
<tr>
<td>Synonyms</td>
<td>ACTIVASE 50mg</td>
</tr>
</tbody>
</table>

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

Use
- pharmaceutical active substance (thrombolytic) *1

1.3. Details of the supplier of the safety data sheet

<table>
<thead>
<tr>
<th>Company information</th>
<th>Enquiries: Genentech, Inc. 1 DNA Way South San Francisco USA-CA 94080 United States of America</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Local representation:</td>
</tr>
<tr>
<td></td>
<td>Phone 001-(650) 225-1000 E-Mail <a href="mailto:info.sds@roche.com">info.sds@roche.com</a> US Chemtrec phone: (800)-424-9300</td>
</tr>
</tbody>
</table>

1.4. Emergency telephone number

<table>
<thead>
<tr>
<th>Emergency telephone number</th>
<th>US Chemtrec phone: (800)-424-9300</th>
</tr>
</thead>
</table>

*1 referring to: Alteplase

**SECTION 2: Hazards identification**

Classification of the substance or mixture / Label elements

<table>
<thead>
<tr>
<th>GHS Classification</th>
<th>no classification and labelling according to GHS</th>
</tr>
</thead>
</table>

Other hazards

| Note               | no information available                          |
**SECTION 3: Composition/information on ingredients**

Characterization
0.5 M arginine phosphate buffer is used as a buffering agent to maintain pH at 7.3.

**Ingredients**

<table>
<thead>
<tr>
<th>Ingredient</th>
<th>Concentration</th>
<th>GHS-Classification</th>
</tr>
</thead>
<tbody>
<tr>
<td>Alteplase</td>
<td>&lt; 2.17 %</td>
<td>(pure ingredient)</td>
</tr>
</tbody>
</table>

*1 referring to: Alteplase

**SECTION 4: First aid measures**

**4.1. Description of first aid measures**

- **Eye contact**
  - rinse immediately with tap water for at least 20 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

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

- **Unsuitable extinguishing media**
  - full water jet

**5.2. Special hazards arising from the substance or mixture**

- **Specific hazards**
  - no particular hazards known
5.3. Advice for firefighters

Protection of fire-fighters
- precipitate gases/vapours/mists with water spray
- use self-contained breathing apparatus

Special method of fire-fighting
- if possible precipitate fire gases with a water jet

SECTION 6: Accidental release measures

6.1. Personal precautions, protective equipment and emergency procedures

Personal precautions
- ensure adequate ventilation

6.2. Environmental precautions

Environmental protection
- do not allow to enter drains or waterways

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

Suitable materials
- glass

7.2. Conditions for safe storage, including any incompatibilities

Storage conditions
- 2 - 30 °C
- protected from light

Validity
- see "best use before" date stated on the label, after opening the content should be used within a short period, any remaining reconstituted solution should be discarded

Packaging materials
- vials

SECTION 8: Exposure controls/personal protection

8.1. Control parameters

Threshold value (USA) air
- STEL: 3 mg/m³ (4 x 15 min) *2
- ACGIH-TLV: 1 mg/m³ *2

Threshold value (Roche) air
- IOEL (Internal Occupational Exposure Limit): 0.2 mg/m³ *1
8.2. Exposure controls

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 (neoprene, nitrile or butyl rubber)

Eye protection
- safety glasses

*1 referring to: Alteplase
*2 referring to: Phosphoric acid

SECTION 9: Physical and chemical properties

9.1. Information on basic physical and chemical properties

Color
- white to off-white

Form
- lyophilized powder

Molecular mass
- ~ 64 kDa

Solubility
- 148'700 mg/l, water (20 °C)

Partition coefficient
- \( \log P_{nw} \cdot 4.20 \) (octanol/water°C)

pH value
- 7.3 (reconstituted solution)

9.2. Other information

Note
- no information available

*1 referring to: Alteplase
*3 referring to: L-Arginine

SECTION 10: Stability and reactivity

10.1. Reactivity

Note
- no information available

10.2. Chemical stability

Stability
- does not contain any antimicrobial preservative; therefore, care must be taken to ensure the sterility of the prepared reconstituted solution
- do not freeze the reconstituted solution

*1 referring to: Alteplase
*3 referring to: L-Arginine
10.3. Possibility of hazardous reactions

Note - no information available

10.4. Conditions to avoid

Conditions to avoid - temperatures above 30 °C
- light

10.5. Incompatible materials

Note - no information available

10.6. Hazardous decomposition products

Note - no information available

SECTION 11: Toxicological information

11.1. Information on toxicological effects

<table>
<thead>
<tr>
<th>Acute toxicity</th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>not bioavailable by oral administration</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>$TD_{lo}$</td>
<td>&gt; 10 mg/kg (i.v., rat)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>$LD_{50}$</td>
<td>1'530 mg/kg (oral, rat)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>$LC_{50}$</td>
<td>&gt; 850 mg/m³ (inhal., rat, 1 h)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>$LD_{50}$</td>
<td>2'740 mg/kg (dermal, rabbit)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>$LD_{50}$</td>
<td>&gt; 5'110 mg/kg (oral, rat)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Subacute toxicity
- $LD_{0}$ 10 mg/kg/d (i.v., several species, 14 d)

Local effects
- skin: non-irritant (rabbit; OECD No. 404)
- eye: not severe irritant or corrosive
- skin: corrosive

Sensitization
anaphylactic reactions may occur following the intravenous application of proteins

Mutagenicity
- does not induce chromosomal aberrations in vitro (OECD No. 473 (Mammalian Cytogenic Test))
- negative (Ames test)
- negative, both with and without metabolic activation (in vitro test system; OECD No. 473 (Mammalian Cytogenic Test))

Carcinogenicity
- no information available

Reproductive toxicity
- Alteplase has been shown to have an embryocidal effect in rabbits when intravenously administered at a dose of 3 mg/kg, which is roughly twice the human dose for acute myocardial infarction

STOT-single exposure
- no information available
ACTIVASE® Vials (50 mg)

STOT-repeated exposure - no information available
Aspiration hazard - no information available
Potential Health Effects - Exposure: Inhalation, Ingestion, Skin contact, Eye contact - Carcinogenicity: not listed by NTP, IARC or OSHA

*1 referring to: Alteplase
*2 referring to: Phosphoric acid
*3 referring to: L-Arginine

SECTION 12: Ecological information

12.1. Toxicity

Ecotoxicity - barely toxic for fish (zebrafish)
LC₅₀ (96 h) 2800 mg/l
NOEC (96 h) 1000 mg/l
(OECD No. 203, semistatic)

- barely toxic for planktonic crustaceans (Daphnia magna)
NOEC (24 h) 1000 mg/l
(OECD No. 202)

- barely toxic for microorganisms (Pseudomonas putida)
EC₁₀ (16 h) > 10000 mg/kg
(DIN 38'412, part 8)

- no information available

- moderately toxic for fish (fish, unspecified)
LC₅₀ 70 mg/l

12.2. Persistence and degradability

Ready biodegradability - globular proteins are generally well biodegradable
- readily biodegradable

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

<table>
<thead>
<tr>
<th>Ref</th>
<th>Referring to</th>
<th>Ingredient</th>
</tr>
</thead>
<tbody>
<tr>
<td>*1</td>
<td></td>
<td>Alteplase</td>
</tr>
<tr>
<td>*2</td>
<td></td>
<td>Phosphoric acid</td>
</tr>
<tr>
<td>*3</td>
<td></td>
<td>L-Arginine</td>
</tr>
</tbody>
</table>

### SECTION 13: Disposal considerations

#### 13.1. Waste treatment methods

Waste from residues
- observe local/national regulations regarding waste disposal

### SECTION 14: Transport information

**Note**
- not classified as Dangerous Good according to the Dangerous Goods Regulations, proper shipping name non-regulated

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

### SECTION 16: Other information

**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 7

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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.