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

1.1. Product identifier

Product name: ACTIVASE® Vials (100 mg)
Product code: SAP-10053301
Synonyms: ACTIVASE 100mg

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

Company information:
Enquiries: Genentech, Inc.
1 DNA Way
South San Francisco
USA-CA 94080
United States of America

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: Alteplase

SECTION 2: Hazards identification

Classification of the substance or mixture / Label elements

GHS Classification: no classification and labelling according to GHS

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>Concentration</th>
<th>GHS-Classification (pure ingredient)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Alteplase</td>
<td>2.17 %</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)
- ACGIH-TLV: 1 mg/m³

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

**Solubility**
- 148’700 mg/l, water (20 °C) *3

**Partition coefficient**
- log \( P_{ow} \) -4.20 (octanol/water°C) *3

**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
### 10. 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>Category</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Acute toxicity</strong></td>
<td></td>
</tr>
<tr>
<td>- TDₜ₀</td>
<td>not bioavailable by oral administration</td>
</tr>
<tr>
<td>- LD₅₀</td>
<td>&gt; 10 mg/kg (i.v., rat)</td>
</tr>
<tr>
<td>- LD₁₀₅₀</td>
<td>1’530 mg/kg (oral, rat)</td>
</tr>
<tr>
<td>- LC₀₅₀</td>
<td>&gt; 850 mg/m³ (inhal., rat, 1 h)</td>
</tr>
<tr>
<td>- LD₀₅₀</td>
<td>2’740 mg/kg (dermal, rabbit)</td>
</tr>
<tr>
<td>- LD₀₅₀</td>
<td>&gt; 5’110 mg/kg (oral, rat)</td>
</tr>
<tr>
<td><strong>Subacute toxicity</strong></td>
<td></td>
</tr>
<tr>
<td>- LD₀</td>
<td>10 mg/kg/d (i.v., several species, 14 d)</td>
</tr>
<tr>
<td><strong>Local effects</strong></td>
<td></td>
</tr>
<tr>
<td>- skin: non-irritant</td>
<td>(rabbit; OECD No. 404)</td>
</tr>
<tr>
<td>- eye: not severe</td>
<td>irritant or corrosive</td>
</tr>
<tr>
<td>- skin: corrosive</td>
<td></td>
</tr>
<tr>
<td><strong>Sensitization</strong></td>
<td>anaphylactic reactions may occur following the intravenous application</td>
</tr>
<tr>
<td></td>
<td>of proteins</td>
</tr>
<tr>
<td><strong>Mutagenicity</strong></td>
<td>does not induce chromosomal aberrations in vitro (OECD No. 473) (Mammalian Cytogenic Test))</td>
</tr>
<tr>
<td></td>
<td>negative (Ames test)</td>
</tr>
<tr>
<td></td>
<td>negative, both with and without metabolic activation (in vitro test</td>
</tr>
<tr>
<td></td>
<td>system; OECD No. 473 (Mammalian Cytogenic Test))</td>
</tr>
<tr>
<td><strong>Carcinogenicity</strong></td>
<td>no information available</td>
</tr>
<tr>
<td><strong>Reproductive toxicity</strong></td>
<td>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</td>
</tr>
<tr>
<td><strong>STOT—single exposure</strong></td>
<td>no information available</td>
</tr>
</tbody>
</table>
## ACTIVASE® Vials (100 mg)

<table>
<thead>
<tr>
<th>STOT-repeated exposure</th>
<th>- no information available</th>
</tr>
</thead>
<tbody>
<tr>
<td>Aspiration hazard</td>
<td>- no information available</td>
</tr>
<tr>
<td>Potential Health Effects</td>
<td>- Exposure: Inhalation, Ingestion, Skin contact, Eye contact</td>
</tr>
<tr>
<td></td>
<td>- Carcinogenicity: not listed by NTP, IARC or OSHA</td>
</tr>
</tbody>
</table>

*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)
  \[ \text{LC}_{50} (96 \text{ h}) \ 2800 \text{ mg/l} \]
  \[ \text{NOEC (96 \text{ h})} \ 1000 \text{ mg/l} \]
  (OECD No. 203, semistatic) *3
- barely toxic for planktonic crustaceans (Daphnia magna)
  \[ \text{NOEC (24 \text{ h})} \ 1000 \text{ mg/l} \]
  (OECD No. 202) *3
- barely toxic for microorganisms (Pseudomonas putida)
  \[ \text{EC}_{10} (16 \text{ h}) > 10000 \text{ mg/kg} \]
  (DIN 38'412, part 8) *3
- no information available *1
- moderately toxic for fish (fish, unspecified)
  \[ \text{LC}_{50} \ 70 \text{ mg/l} \] *2

#### 12.2. Persistence and degradability

**Ready biodegradability**
- globular proteins are generally well biodegradable *1
- readily biodegradable *3

#### 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

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

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

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.