ACTIVASE® Vials (100 mg)

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

Emergency Overview

Form lyophilized powder
Color white to off-white

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</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Alteplase</strong></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
ACTIVASE® Vials (100 mg)

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 - 8 °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

<table>
<thead>
<tr>
<th>Threshold value (USA) air</th>
<th>STEL: 3 mg/m³ (4 x 15 min) *2</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>ACGIH-TLV: 1 mg/m³ *2</td>
</tr>
</tbody>
</table>

| 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

<table>
<thead>
<tr>
<th>Property</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Color</td>
<td>white to off-white</td>
</tr>
<tr>
<td>Form</td>
<td>lyophilized powder</td>
</tr>
<tr>
<td>Molecular mass</td>
<td>~ 64 kDa</td>
</tr>
<tr>
<td>Solubility</td>
<td>148'700 mg/l, water (20 °C)</td>
</tr>
<tr>
<td>Partition coefficient</td>
<td>log P_{ow} -4.20 (octanol/water*°C)</td>
</tr>
<tr>
<td>pH value</td>
<td>7.3 (reconstituted solution)</td>
</tr>
</tbody>
</table>

9.2. Other information

Note - no information available

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

*1 *3 referring to: Alteplase

Date: 25.2.16/LS (SEISMO)  Replacing edition of: 24.2.16  Page: 4/8
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

10.3. 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

Acute toxicity
- not bioavailable by oral administration
- TD\textsubscript{lo} > 10 mg/kg (i.v., rat) \textsuperscript{1}
- LD\textsubscript{50} 1'530 mg/kg (oral, rat) \textsuperscript{2}
- LC\textsubscript{50} > 850 mg/m\textsuperscript{3} (inhal., rat, 1 h) \textsuperscript{2}
- LD\textsubscript{50} 2'740 mg/kg (dermal, rabbit) \textsuperscript{2}
- LD\textsubscript{50} > 5'110 mg/kg (oral, rat) \textsuperscript{3}

Subacute toxicity
- LD\textsubscript{0} 10 mg/kg/d (i.v., several species, 14 d) \textsuperscript{1}

Local effects
- skin: non-irritant (rabbit; OECD No. 404) \textsuperscript{3}
- eye: not severe irritant or corrosive \textsuperscript{3}
- skin: corrosive \textsuperscript{2}

Sensitization
anaphylactic reactions may occur following the intravenous application of proteins \textsuperscript{1}
## 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

## 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)  
  \[ LC_{50} \ (96 \ h) \ 2800 \ mg/l \]
  \[ NOEC \ (96 \ h) \ 1000 \ mg/l \]
  (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)  
  \[ EC_{10} \ (16 \ h) > 10000 \ mg/kg \]
  (DIN 38 412, part 8)  
- no information available
- moderately toxic for fish (fish, unspecified)  
  \[ LC_{50} \ 70 \ mg/l \]

#### 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

*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 (1-609-292-5560) 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 2, 4, 5, 6, 12

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.