SAFETY DATA SHEET

RITUXAN HYCELA(TM) Vials (1,400 mg/23,400 Units per 11.7 ml)

Version 1.3
Revision Date: 04-26-2021
Date of last issue: 02-10-2020
Date of first issue: 06-10-2017

SECTION 1. IDENTIFICATION

Product name: RITUXAN HYCELA(TM) Vials (1,400 mg/23,400 Units per 11.7 ml)
Product code: RO045-2294/F04

Manufacturer or supplier's details
Company name of supplier: Genentech, Inc.
Address: 1 DNA Way South San Francisco, CA 94080 USA
Telephone: 001-(650) 225-1000
E-mail address: info.sds@roche.com
Emergency telephone number: US Chemtrec phone (800)-424-9300

Recommended use of the chemical and restrictions on use
Recommended use: Formulated pharmaceutical active substance
Restrictions on use: For professional users only.

SECTION 2. HAZARDS IDENTIFICATION

GHS classification in accordance with the OSHA Hazard Communication Standard (29 CFR 1910.1200)
Not a hazardous substance or mixture.

GHS label elements
Not a hazardous substance or mixture.

Other hazards
None known.

SECTION 3. COMPOSITION/INFORMATION ON INGREDIENTS

Substance / Mixture: Mixture

Components

<table>
<thead>
<tr>
<th>Chemical name</th>
<th>CAS-No.</th>
<th>Concentration (% w/w)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rituximab</td>
<td>174722-31-7</td>
<td>12.0</td>
</tr>
<tr>
<td>Hyaluronidase</td>
<td>757971-58-7</td>
<td>0.003</td>
</tr>
<tr>
<td>Trehalose (D+)-, 2H2O</td>
<td>6138-23-4</td>
<td>7.92</td>
</tr>
<tr>
<td>L-Histidine monohydrochloride monohydrate</td>
<td>5934-29-2</td>
<td>0.35</td>
</tr>
<tr>
<td>L-Histidine</td>
<td>71-00-1</td>
<td>0.05</td>
</tr>
<tr>
<td>L-Methionine</td>
<td>63-68-3</td>
<td>0.15</td>
</tr>
</tbody>
</table>
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<table>
<thead>
<tr>
<th>Substance</th>
<th>CAS Number</th>
<th>Amount</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sorbitan, mono-(9Z)-9-octadecenoate, poly(oxy-1,2-ethanediyl) derivs.</td>
<td>9005-65-6</td>
<td>0.06</td>
</tr>
<tr>
<td>Water</td>
<td>7732-18-5</td>
<td>&gt; 79.0</td>
</tr>
</tbody>
</table>

SECTION 4. FIRST AID MEASURES

General advice : Do not leave the victim unattended.

If inhaled : Move to fresh air.
If unconscious, place in recovery position and seek medical advice.
If symptoms persist, call a physician.

In case of skin contact : If on skin, rinse well with water.

In case of eye contact : Immediately flush eye(s) with plenty of water.
Remove contact lenses.
Protect unharmed eye.
If eye irritation persists, consult a specialist.

If swallowed : Keep respiratory tract clear.
Do not give milk or alcoholic beverages.
Never give anything by mouth to an unconscious person.
If symptoms persist, call a physician.
Rinse mouth with water.

Most important symptoms and effects, both acute and delayed : None known.

Notes to physician : The first aid procedure should be established in consultation with the doctor responsible for industrial medicine.

SECTION 5. FIRE-FIGHTING MEASURES

Suitable extinguishing media : Use extinguishing measures that are appropriate to local circumstances and the surrounding environment.

Specific hazards during fire fighting : No information available.

Hazardous combustion products : In case of fire hazardous decomposition products may be produced such as:
Carbon oxides
Nitrogen oxides (NOx)

Further information : Standard procedure for chemical fires.
Use extinguishing measures that are appropriate to local circumstances and the surrounding environment.

Special protective equipment for fire-fighters : Wear self-contained breathing apparatus for firefighting if necessary.
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SECTION 6. ACCIDENTAL RELEASE MEASURES

Personal precautions, protective equipment and emergency procedures
: Refer to protective measures listed in sections 7 and 8.

Environmental precautions
: Local authorities should be advised if significant spillages cannot be contained.

Methods and materials for containment and cleaning up
: Wipe up with absorbent material (e.g. cloth, fleece).
: Keep in suitable, closed containers for disposal.

SECTION 7. HANDLING AND STORAGE

Advice on protection against fire and explosion
: Normal measures for preventive fire protection.

Advice on safe handling
: For personal protection see section 8.
: Smoking, eating and drinking should be prohibited in the application area.

Conditions for safe storage
: Electrical installations / working materials must comply with the technological safety standards.

Further information on storage conditions
: See label, package insert or internal guidelines

Materials to avoid
: No materials to be especially mentioned.

Storage temperature
: Protected from heat and light

Further information on storage stability
: No decomposition if stored and applied as directed.

Packaging material
: Suitable material: Stainless steel, glass, Vials

SECTION 8. EXPOSURE CONTROLS/PERSONAL PROTECTION

Ingredients with workplace control parameters

<table>
<thead>
<tr>
<th>Components</th>
<th>CAS-No.</th>
<th>Value type (Form of exposure)</th>
<th>Control parameters / Permissible concentration</th>
<th>Basis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rituximab</td>
<td>174722-31-7</td>
<td>IOEL</td>
<td>0.04 mg/m3</td>
<td>Roche Industrial Hygiene Committee (RIHC)</td>
</tr>
<tr>
<td>Hyaluronidase</td>
<td>757971-58-7</td>
<td>IOEL</td>
<td>0.00006 mg/m3</td>
<td>Roche Industrial</td>
</tr>
</tbody>
</table>
SAFETY DATA SHEET

RITUXAN HYCELA(TM) Vials (1,400 mg/23,400 Units per 11.7 ml)

<table>
<thead>
<tr>
<th>Engineering measures</th>
<th>Personal protective equipment</th>
<th></th>
<th>Hygiene Committee (RIHC)</th>
</tr>
</thead>
<tbody>
<tr>
<td>:</td>
<td>:</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Engineering measures**: No data available

**Personal protective equipment**

Respiratory protection : No personal respiratory protective equipment normally required.

Hand protection

In case of contact through splashing:

- Material : Nitrile rubber
- Break through time : > 30 min
- Glove thickness : > 0.11 mm

In case of full contact:

- Material : butyl-rubber
- Break through time : > 480 min
- Glove thickness : > 0.4 mm

Remarks : Wear appropriate protective gloves to prevent skin contact. Replace torn or punctured gloves promptly.

Eye protection : Safety glasses

Skin and body protection : Protective suit

Hygiene measures : Handle in accordance with good industrial hygiene and safety practice.

**SECTION 9. PHYSICAL AND CHEMICAL PROPERTIES**

**Appearance** : Clear liquid, Sterile liquid

**Color** : colorless, light yellow

**Odor** : No data available

**Odor Threshold** : No data available

**pH** : 5.0 - 6.0

**Melting point/range** : No data available

**Boiling point/boiling range** : No data available

**Evaporation rate** : No data available
SAFETY DATA SHEET

RITUXAN HYCELA(TM) Vials (1,400 mg/23,400 Units per 11.7 ml)

SECTION 10. STABILITY AND REACTIVITY

Reactivity : No dangerous reaction known under conditions of normal use.

Chemical stability : Stable under normal conditions.

Proteins are temperature-sensitive; the thermal denaturation has an impact on quality but does not affect Plant and Process Safety; during decomposition no flammable gas, no organic peroxide and no oxidising substances are created

Possibility of hazardous reactions : Stable under recommended storage conditions. No hazards to be specially mentioned.

Incompatible materials : No data available

Hazardous decomposition products : No data available

SECTION 11. TOXICOLOGICAL INFORMATION

Acute toxicity
Not classified based on available information.
Components:

Rituximab:
Acute oral toxicity: Remarks: Not bioavailable by oral administration
Acute toxicity (other routes of administration): Maximum tolerated dose (Mouse): > 100 mg/kg Application Route: i.p.

Hyaluronidase:
Acute oral toxicity: Remarks: Not bioavailable by oral administration
Skin corrosion/irritation
Not classified based on available information.

Components:
Hyaluronidase:
Remarks: This information is not available.

Serious eye damage/eye irritation
Not classified based on available information.

Components:
Hyaluronidase:
Remarks: This information is not available.

Respiratory or skin sensitization
Skin sensitization
Not classified based on available information.
Respiratory sensitization
Not classified based on available information.

Components:
Hyaluronidase:
Remarks: May cause sensitization of susceptible persons by skin contact or by inhalation of dust.

Germ cell mutagenicity
Not classified based on available information.
Carcinogenicity
Not classified based on available information.
IARC No ingredient of this product present at levels greater than or equal to 0.1% is identified as probable, possible or confirmed human carcinogen by IARC.
OSHA No component of this product present at levels greater than or equal to 0.1% is on OSHA’s list of regulated carcinogens.
NTP No ingredient of this product present at levels greater than or equal to 0.1% is
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identified as a known or anticipated carcinogen by NTP.

Reproductive toxicity
Not classified based on available information.

STOT-single exposure
Not classified based on available information.

Components:

Hyaluronidase:
Assessment : The substance or mixture is not classified as specific target organ toxicant, single exposure.

STOT-repeated exposure
Not classified based on available information.

Components:

Hyaluronidase:
Assessment : The substance or mixture is not classified as specific target organ toxicant, repeated exposure.

Repeated dose toxicity

Components:

Hyaluronidase:
Species : cynomolgus monkey
NOAEL : 2 mg/kg/w
Application Route : s.c.
Exposure time : 39 weeks

Aspiration toxicity
Not classified based on available information.

Components:

Hyaluronidase:
No data available

Further information

Components:

Rituximab:
Remarks : Globular proteins are generally well biodegradable
SECTION 12. ECOLOGICAL INFORMATION

Ecotoxicity

Components:

Hyaluronidase:
Ecotoxicology Assessment
Toxicity Data on Soil : Not expected to adsorb on soil.
Other organisms relevant to the environment : No data available

Persistence and degradability

Components:

Rituximab:
Biodegradability : Result: Globular proteins are generally well biodegradable

Hyaluronidase:
Biodegradability : Result: Globular proteins are generally well biodegradable

Bioaccumulative potential

Components:

Rituximab:
Partition coefficient: n-octanol/water : Remarks: No data available

Hyaluronidase:
Partition coefficient: n-octanol/water : Remarks: No data available

Mobility in soil
No data available

Other adverse effects

Product:
Ozone-Depletion Potential : Regulation: 40 CFR Protection of Environment; Part 82 Protection of Stratospheric Ozone - CAA Section 602 Class I Substances Remarks: This product neither contains, nor was manufactured with a Class I or Class II ODS as defined by the U.S. Clean Air Act Section 602 (40 CFR 82, Subpt. A, App.A + B).
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Components:

Rituximab:
Additional ecological information: Monoclonal antibodies are proteins with highly specific affinity to a certain antigen; therefore, no appreciable ecotoxic potential is to be expected

Hyaluronidase:
Additional ecological information: No data available

SECTION 13. DISPOSAL CONSIDERATIONS

Disposal methods
Waste from residues: Can be disposed as waste water, when in compliance with local regulations.
Contaminated packaging: Empty containers should be taken to an approved waste handling site for recycling or disposal. Do not re-use empty containers.

SECTION 14. TRANSPORT INFORMATION

International Regulations

UNRTDG
Not regulated as a dangerous good

IATA-DGR
Not regulated as a dangerous good

IMDG-Code
Not regulated as a dangerous good

Transport in bulk according to Annex II of MARPOL 73/78 and the IBC Code
Not applicable

Domestic regulation

49 CFR
Not regulated as a dangerous good

SECTION 15. REGULATORY INFORMATION

CERCLA Reportable Quantity
This material does not contain any components with a CERCLA RQ.

SARA 304 Extremely Hazardous Substances Reportable Quantity
This material does not contain any components with a section 304 EHS RQ.
SARA 302 Extremely Hazardous Substances Threshold Planning Quantity
This material does not contain any components with a section 302 EHS TPQ.

SARA 311/312 Hazards : No SARA Hazards

SARA 313 : This material does not contain any chemical components with known CAS numbers that exceed the threshold (De Minimis) reporting levels established by SARA Title III, Section 313.

Clean Air Act
This product neither contains, nor was manufactured with a Class I or Class II ODS as defined by the U.S. Clean Air Act Section 602 (40 CFR 82, Subpt. A, App.A + B).
This product does not contain any hazardous air pollutants (HAP), as defined by the U.S. Clean Air Act Section 112 (40 CFR 61).
This product does not contain any chemicals listed under the U.S. Clean Air Act Section 112(r) for Accidental Release Prevention (40 CFR 68.130, Subpart F).
This product does not contain any chemicals listed under the U.S. Clean Air Act Section 111 SOC Mi Intermediate or Final VOC's (40 CFR 60.489).

Clean Water Act
This product does not contain any Hazardous Substances listed under the U.S. Clean Water Act, Section 311, Table 116.4A.
This product does not contain any Hazardous Chemicals listed under the U.S. Clean Water Act, Section 311, Table 117.3.
This product does not contain any toxic pollutants listed under the U.S. Clean Water Act Section 307
This product does not contain any priority pollutants related to the U.S. Clean Water Act

US State Regulations
Massachusetts Right To Know
No components are subject to the Massachusetts Right to Know Act.

Pennsylvania Right To Know
Water 7732-18-5
Rituximab 174722-31-7
Trehalose (D+)-), 2H2O 6138-23-4

Maine Chemicals of High Concern
Hyaluronidase 757971-58-7

Vermont Chemicals of High Concern
Hyaluronidase 757971-58-7

Washington Chemicals of High Concern
Hyaluronidase 757971-58-7

The ingredients of this product are reported in the following inventories:
AIIC : Not in compliance with the inventory

DSL : This product contains the following components that are not on the Canadian DSL nor NDSL.

Rituximab
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L-Histidine monohydrochloride monohydrate
Hyaluronidase

NZIoC: On the inventory, or in compliance with the inventory
ENCS: Not in compliance with the inventory
ISHL: Not in compliance with the inventory
KECI: Not in compliance with the inventory
PICCS: Not in compliance with the inventory
IECSC: Not in compliance with the inventory
TCSI: Not in compliance with the inventory
TSCA: Product contains substance(s) not listed on TSCA inventory.

TSCA list
No substances are subject to a Significant New Use Rule.

No substances are subject to TSCA 12(b) export notification requirements.

SECTION 16. OTHER INFORMATION

NFPA 704:

<table>
<thead>
<tr>
<th>Flammability</th>
<th>Health</th>
<th>Instability</th>
<th>Special hazard</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
</tbody>
</table>

HMIS® IV:

<table>
<thead>
<tr>
<th>HEALTH</th>
<th>FLAMMABILITY</th>
<th>PHYSICAL HAZARD</th>
</tr>
</thead>
<tbody>
<tr>
<td>/</td>
<td>0</td>
<td>0</td>
</tr>
</tbody>
</table>

HMIS® ratings are based on a 0-4 rating scale, with 0 representing minimal hazards or risks, and 4 representing significant hazards or risks. The "*" represents a chronic hazard, while the "/" represents the absence of a chronic hazard.

Full text of other abbreviations
The information provided in this Safety Data Sheet is correct to the best of our knowledge, information and belief at the date of its publication. The information given is designed only as a guidance for safe handling, use, processing, storage, transportation, disposal and release and is not to be considered a warranty or quality specification. The information relates only to the specific material designated and may not be valid for such material used in combination with any other materials or in any process, unless specified in the text.

Revision Date : 04-26-2021

US / Z8 / 2004