SAFETY DATA SHEET
according to Regulation (EC) No. 1907/2006

Rizatriptan Formulation

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

1.1 Product identifier
   Trade name : Rizatriptan Formulation

1.2 Relevant identified uses of the substance or mixture and uses advised against
   Use of the Substance/Mixture : Pharmaceutical

1.3 Details of the supplier of the safety data sheet
   Company : MSD
   Shotton Lane
   NE23 3JU Cramlington NU - Great Britain
   Telephone : 44 1 670 59 30 00
   Telefax : 908-735-1496
   E-mail address of person responsible for the SDS : EHSDATASTEWARD@msd.com

1.4 Emergency telephone number
   1-908-423-6000

SECTION 2: Hazards identification

2.1 Classification of the substance or mixture
   Classification (REGULATION (EC) No 1272/2008)
   Reproductive toxicity, Category 2 : H361d: Suspected of damaging the unborn child.
   Specific target organ toxicity - repeated exposure, Category 2 : H373: May cause damage to organs through prolonged or repeated exposure.

2.2 Label elements
   Labelling (REGULATION (EC) No 1272/2008)
   Hazard pictograms :
   Signal word : Warning
   Hazard statements : H361d Suspected of damaging the unborn child.
                     H373 May cause damage to organs through prolonged or repeated exposure.
   Precautionary statements : Prevention:
                            P201 Obtain special instructions before use.
Hazardous components which must be listed on the label:
Rizatriptan

2.3 Other hazards
Dust contact with the eyes can lead to mechanical irritation.
Contact with dust can cause mechanical irritation or drying of the skin.
May form explosive dust-air mixture during processing, handling or other means.

SECTION 3: Composition/information on ingredients

3.2 Mixtures

<table>
<thead>
<tr>
<th>Components</th>
<th>CAS-No.</th>
<th>EC-No.</th>
<th>Index-No.</th>
<th>Registration number</th>
<th>Classification</th>
<th>Concentration (% w/w)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rizatriptan</td>
<td>145202-66-0</td>
<td></td>
<td></td>
<td></td>
<td>Acute Tox.4; H302 Eye Irrit.2; H319 Repr.2; H361d STOT SE3; H336 STOT RE1; H372</td>
<td>&gt;= 3 - &lt; 10</td>
</tr>
</tbody>
</table>

For explanation of abbreviations see section 16.

SECTION 4: First aid measures

4.1 Description of first aid measures

General advice
In the case of accident or if you feel unwell, seek medical advice immediately.
When symptoms persist or in all cases of doubt seek medical advice.

Protection of first-aiders
First Aid responders should pay attention to self-protection, and use the recommended personal protective equipment when the potential for exposure exists (see section 8).

If inhaled
If inhaled, remove to fresh air.
Get medical attention.

In case of skin contact
In case of contact, immediately flush skin with soap and plenty of water.
Remove contaminated clothing and shoes.
Get medical attention.  
Wash clothing before reuse.  
Thoroughly clean shoes before reuse.

In case of eye contact:  
If in eyes, rinse well with water.  
Get medical attention if irritation develops and persists.  

If swallowed:  
If swallowed, DO NOT induce vomiting.  
Get medical attention.  
Rinse mouth thoroughly with water.

4.2 Most important symptoms and effects, both acute and delayed

Risks:  
Suspected of damaging the unborn child.  
May cause damage to organs through prolonged or repeated exposure.  
Contact with dust can cause mechanical irritation or drying of the skin.  
Dust contact with the eyes can lead to mechanical irritation.

4.3 Indication of any immediate medical attention and special treatment needed

Treatment:  
Treat symptomatically and supportively.

SECTION 5: Firefighting measures

5.1 Extinguishing media

Suitable extinguishing media:  
Water spray  
Alcohol-resistant foam  
Carbon dioxide (CO2)  
Dry chemical

Unsuitable extinguishing media:  
None known.

5.2 Special hazards arising from the substance or mixture

Specific hazards during firefighting:  
Avoid generating dust; fine dust dispersed in air in sufficient concentrations, and in the presence of an ignition source is a potential dust explosion hazard.  
Exposure to combustion products may be a hazard to health.

Hazardous combustion products:  
Carbon oxides

5.3 Advice for firefighters

Special protective equipment for firefighters:  
In the event of fire, wear self-contained breathing apparatus.  
Use personal protective equipment.

Specific extinguishing methods:  
Use extinguishing measures that are appropriate to local circumstances and the surrounding environment.
Use water spray to cool unopened containers.
Remove undamaged containers from fire area if it is safe to do so.
Evacuate area.

SECTION 6: Accidental release measures

6.1 Personal precautions, protective equipment and emergency procedures

Personal precautions: Use personal protective equipment. Follow safe handling advice and personal protective equipment recommendations.

6.2 Environmental precautions

Environmental precautions: Discharge into the environment must be avoided. Prevent further leakage or spillage if safe to do so. Retain and dispose of contaminated wash water. Local authorities should be advised if significant spillages cannot be contained.

6.3 Methods and material for containment and cleaning up

Methods for cleaning up: Sweep up or vacuum up spillage and collect in suitable container for disposal. Avoid dispersal of dust in the air (i.e., clearing dust surfaces with compressed air). Dust deposits should not be allowed to accumulate on surfaces, as these may form an explosive mixture if they are released into the atmosphere in sufficient concentration. Local or national regulations may apply to releases and disposal of this material, as well as those materials and items employed in the cleanup of releases. You will need to determine which regulations are applicable. Sections 13 and 15 of this SDS provide information regarding certain local or national requirements.

6.4 Reference to other sections
See sections: 7, 8, 11, 12 and 13.

SECTION 7: Handling and storage

7.1 Precautions for safe handling

Technical measures: Static electricity may accumulate and ignite suspended dust causing an explosion. Provide adequate precautions, such as electrical grounding and bonding, or inert atmospheres.

Local/Total ventilation: Use only with adequate ventilation.

Advice on safe handling: Do not breathe dust. Do not swallow. Avoid contact with eyes. Avoid prolonged or repeated contact with skin. Handle in accordance with good industrial hygiene and safety
practice, based on the results of the workplace exposure assessment
Minimize dust generation and accumulation.
Keep container closed when not in use.
Keep away from heat and sources of ignition.
Take precautionary measures against static discharges.
Take care to prevent spills, waste and minimize release to the environment.

Hygiene measures:
If exposure to chemical is likely during typical use, provide eye flushing systems and safety showers close to the working place. When using do not eat, drink or smoke. Wash contaminated clothing before re-use.
The effective operation of a facility should include review of engineering controls, proper personal protective equipment, appropriate degowning and decontamination procedures, industrial hygiene monitoring, medical surveillance and the use of administrative controls.

7.2 Conditions for safe storage, including any incompatibilities
Requirements for storage areas and containers:
Keep in properly labelled containers. Store locked up. Store in accordance with the particular national regulations.

Advice on common storage:
Do not store with the following product types:
- Strong oxidizing agents
- Organic peroxides
- Explosives
- Gases

7.3 Specific end use(s)
Specific use(s):
No data available

SECTION 8: Exposure controls/personal protection

8.1 Control parameters

<table>
<thead>
<tr>
<th>Components</th>
<th>CAS-No.</th>
<th>Value type (Form of exposure)</th>
<th>Control parameters</th>
<th>Basis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rizatriptan</td>
<td>145202-66-0</td>
<td>TWA</td>
<td>10 µg/m³ (OEB 3)</td>
<td>Internal</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Wipe limit</td>
<td>100 µg/100 cm²</td>
<td>Internal</td>
</tr>
</tbody>
</table>

8.2 Exposure controls

Engineering measures
All engineering controls should be implemented by facility design and operated in accordance with GMP principles to protect products, workers, and the environment.
Containment technologies suitable for controlling compounds are required to control at source and to prevent migration of the compound to uncontrolled areas (e.g., open-face containment devices).
Minimize open handling.
Personal protective equipment

Eye protection: Wear safety glasses with side shields or goggles. If the work environment or activity involves dusty conditions, mists or aerosols, wear the appropriate goggles. Wear a faceshield or other full face protection if there is a potential for direct contact to the face with dusts, mists, or aerosols.

Hand protection

Material: Chemical-resistant gloves
Remarks: Consider double gloving.

Skin and body protection

Work uniform or laboratory coat. Additional body garments should be used based upon the task being performed (e.g., sleevelets, apron, gauntlets, disposable suits) to avoid exposed skin surfaces. Use appropriate degowning techniques to remove potentially contaminated clothing.

Respiratory protection: If adequate local exhaust ventilation is not available or exposure assessment demonstrates exposures outside the recommended guidelines, use respiratory protection.

Filter type: Particulates type (P)

SECTION 9: Physical and chemical properties

9.1 Information on basic physical and chemical properties

Appearance: powder
Colour: pink
Odour: odourless
Odour Threshold: No data available
pH: No data available
Melting point/freezing point: No data available
Initial boiling point and boiling range: No data available
Flash point: Not applicable
Evaporation rate: No data available
Flammability (solid, gas): May form explosive dust-air mixture during processing, handling or other means.
Upper explosion limit / Upper flammability limit: No data available
Lower explosion limit / Lower flammability limit: No data available
Vapour pressure: No data available
Relative vapour density: No data available
SECTION 10: Stability and reactivity

10.1 Reactivity
Not classified as a reactivity hazard.

10.2 Chemical stability
Stable under normal conditions.

10.3 Possibility of hazardous reactions
Hazardous reactions: May form explosive dust-air mixture during processing, handling or other means. Can react with strong oxidizing agents.

10.4 Conditions to avoid
Conditions to avoid: Heat, flames and sparks. Avoid dust formation.

10.5 Incompatible materials
Materials to avoid: Oxidizing agents

10.6 Hazardous decomposition products
No hazardous decomposition products are known.
SECTION 11: Toxicological information

11.1 Information on toxicological effects

Information on likely routes of exposure:
- Inhalation
- Skin contact
- Ingestion
- Eye contact

**Acute toxicity**
Not classified based on available information.

**Product:**
- Acute oral toxicity: Acute toxicity estimate: > 2.000 mg/kg
  Method: Calculation method

**Components:**

- **Rizatriptan:**
  - Acute oral toxicity: LD50 (Rat): 2.227 mg/kg
    LD50 (Mouse): 700 - 1.631 mg/kg

**Skin corrosion/irritation**
Not classified based on available information.

**Components:**

- **Rizatriptan:**
  - Species: Rabbit
  - Result: No skin irritation

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

**Components:**

- **Rizatriptan:**
  - Species: Bovine cornea
  - Remarks: Moderate eye irritation

**Respiratory or skin sensitisation**

**Skin sensitisation**
Not classified based on available information.

**Respiratory sensitisation**
Not classified based on available information.

**Components:**

- **Rizatriptan:**
  - Test Type: Maximisation Test
### Exposure routes
- **Species**: Guinea pig
- **Assessment**: Does not cause skin sensitisation.
- **Result**: negative

### Germ cell mutagenicity
Not classified based on available information.

### Components:

#### Rizatriptan:

- **Genotoxicity in vitro**
  - **Test Type**: Bacterial reverse mutation assay (AMES)
  - **Result**: negative
  - **Test Type**: Alkaline elution assay
  - **Result**: negative
  - **Test Type**: In vitro mammalian cell gene mutation test
  - **Result**: negative
  - **Test Type**: Chromosome aberration test in vitro
  - **Result**: negative

- **Genotoxicity in vivo**
  - **Test Type**: Mammalian erythrocyte micronucleus test (in vivo cytogenetic assay)
  - **Species**: Mouse
  - **Application Route**: Oral
  - **Result**: negative

### Carcinogenicity
Not classified based on available information.

### Components:

#### Rizatriptan:

- **Species**: Mouse
- **Application Route**: Oral
- **Exposure time**: 100 weeks
- **NOAEL**: 125 mg/kg body weight
- **Result**: negative

- **Species**: Rat
- **Application Route**: Oral
- **Exposure time**: 106 weeks
- **NOAEL**: 106 mg/kg body weight
- **Result**: negative

### Reproductive toxicity
Suspected of damaging the unborn child.

### Components:

#### Rizatriptan:
Rizatriptan Formulation

Effects on fertility

- **Test Type**: Fertility/early embryonic development
- **Species**: Rat, female
- **Application Route**: Oral
- **Fertility**: LOAEL: 100 mg/kg body weight
- **Symptoms**: altered estrus cycles
- **Result**: No effects on fertility and early embryonic development were detected.

- **Test Type**: Fertility/early embryonic development
- **Species**: Rat, male
- **Application Route**: Oral
- **Fertility**: NOAEL: 250 mg/kg body weight
- **Result**: No effects on fertility and early embryonic development were detected.

Effects on foetal development

- **Test Type**: Embryo-foetal development
- **Species**: Rat
- **Application Route**: Oral
- **Developmental Toxicity**: LOAEL: 10 mg/kg body weight
- **Result**: No teratogenic effects, Embryo-foetal toxicity

- **Test Type**: Embryo-foetal development
- **Species**: Rabbit
- **Application Route**: Oral
- **Developmental Toxicity**: LOAEL: 100 mg/kg body weight
- **Result**: No teratogenic effects, Embryo-foetal toxicity

Remarks: The effects were seen only at maternally toxic doses.

Reproductive toxicity - Assessment

- Some evidence of adverse effects on development, based on animal experiments.

STOT - single exposure

- Not classified based on available information.

Components:

**Rizatriptan**

- **Assessment**: May cause drowsiness or dizziness.

STOT - repeated exposure

- May cause damage to organs through prolonged or repeated exposure.

Components:

**Rizatriptan**

- **Target Organs**: Cardio-vascular system
- **Assessment**: Causes damage to organs through prolonged or repeated exposure.
Repeated dose toxicity

Components:

Rizatriptan:
Species: Rat
LOAEL: 1 mg/kg
Application Route: Oral
Exposure time: 14 Weeks
Symptoms: Dilatation of the pupil, Increased pulse rate, Redness

Species: Dog
LOAEL: 0.05 mg/kg
Application Route: Intravenous
Exposure time: 2 Weeks
Symptoms: Dilatation of the pupil, Increased pulse rate, Redness

Species: Dog
LOAEL: 0.2 mg/kg
Application Route: Oral
Exposure time: 1 yr
Symptoms: Dilatation of the pupil

Aspiration toxicity
Not classified based on available information.

Experience with human exposure

Components:

Rizatriptan:
Ingestion: Target Organs: Cardio-vascular system
Symptoms: asthenia, Fatigue, Pain, Dizziness, Weakness, Drowsiness

SECTION 12: Ecological information

12.1 Toxicity

Components:

Rizatriptan:
Toxicity to fish: LC50 (Pimephales promelas (fathead minnow)): > 1.000 mg/l
Exposure time: 96 h

Toxicity to daphnia and other aquatic invertebrates: EC50 (Daphnia magna (Water flea)): 1.000 mg/l
Exposure time: 48 h

Toxicity to algae/aquatic plants: EC50 (Pseudokirchneriella subcapitata (green algae)): > 100 mg/l
Exposure time: 72 h
Method: OECD Test Guideline 201
NOEC (Pseudokirchneriella subcapitata (green algae)): 48
Rizatriptan Formulation

12.2 Persistence and degradability

Components:

Rizatriptan:


12.3 Bioaccumulative potential

Components:

Rizatriptan:

Partition coefficient: n-octanol/water: log Pow: -0.649

12.4 Mobility in soil

Components:

Rizatriptan:

Distribution among environmental compartments: log Koc: 3.83 Method: OECD Test Guideline 106

12.5 Results of PBT and vPvB assessment

Not relevant
SAFETY DATA SHEET
according to Regulation (EC) No. 1907/2006

Rizatriptan Formulation

12.6 Other adverse effects
No data available

SECTION 13: Disposal considerations

13.1 Waste treatment methods

<table>
<thead>
<tr>
<th>Product</th>
<th>Dispose of in accordance with local regulations. According to the European Waste Catalogue, Waste Codes are not product specific, but application specific. Waste codes should be assigned by the user, preferably in discussion with the waste disposal authorities.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Contaminated packaging</td>
<td>Empty containers should be taken to an approved waste handling site for recycling or disposal. If not otherwise specified: Dispose of as unused product.</td>
</tr>
</tbody>
</table>

SECTION 14: Transport information

14.1 UN number
Not regulated as a dangerous good

14.2 UN proper shipping name
Not regulated as a dangerous good

14.3 Transport hazard class(es)
Not regulated as a dangerous good

14.4 Packing group
Not regulated as a dangerous good

14.5 Environmental hazards
Not regulated as a dangerous good

14.6 Special precautions for user
Not applicable

14.7 Transport in bulk according to Annex II of Marpol and the IBC Code
Remarks: Not applicable for product as supplied.

SECTION 15: Regulatory information

15.1 Safety, health and environmental regulations/legislation specific for the substance or mixture

| Regulation (EC) No 1005/2009 on substances that deplete the ozone layer | Not applicable |
| Regulation (EC) No 850/2004 on persistent organic pollutants | Not applicable |
| REACH - Restrictions on the manufacture, placing on the market and use of certain dangerous substances, preparations and articles (Annex XVII) | Not applicable |
| REACH - Candidate List of Substances of Very High Concern for Authorisation (Article 59). | Not applicable |
| REACH - List of substances subject to authorisation (Annex XIV) | Not applicable |
| REACH - Restrictions on the manufacture, placing on the market and use of certain dangerous substances, preparations and articles (Annex XVII) | Not applicable |
SAFETY DATA SHEET
according to Regulation (EC) No. 1907/2006

Rizatriptan Formulation

<table>
<thead>
<tr>
<th>Version</th>
<th>Revision Date:</th>
<th>SDS Number:</th>
<th>Date of last issue:</th>
<th>Date of first issue:</th>
</tr>
</thead>
</table>

Regulation (EC) No 649/2012 of the European Parliament and the Council concerning the export and import of dangerous chemicals:
Not applicable

Other regulations:
Take note of Directive 92/85/EEC regarding maternity protection or stricter national regulations, where applicable.
Young people under the age of 18 are not allowed to use or be exposed to the product professionally. Young people above the age of 15 are, however, except from this rule if the product is a necessary part of their education.

The components of this product are reported in the following inventories:
AICS: not determined
DSL: not determined
IECSC: not determined

15.2 Chemical safety assessment
A Chemical Safety Assessment has not been carried out.

SECTION 16: Other information

Other information:
Items where changes have been made to the previous version are highlighted in the body of this document by two vertical lines.

Full text of H-Statements
H302: Harmful if swallowed.
H319: Causes serious eye irritation.
H336: May cause drowsiness or dizziness.
H361d: Suspected of damaging the unborn child.
H372: Causes damage to organs through prolonged or repeated exposure if swallowed.

Full text of other abbreviations
Acute Tox.: Acute toxicity
Eye Irrit.: Eye irritation
Repr.: Reproductive toxicity
STOT RE: Specific target organ toxicity - repeated exposure
STOT SE: Specific target organ toxicity - single exposure

ADN - European Agreement concerning the International Carriage of Dangerous Goods by Inland Waterways; ADR - European Agreement concerning the International Carriage of Dangerous Goods by Road; AICS - Australian Inventory of Chemical Substances; ASTM - American Society for the Testing of Materials; bw - Body weight; CLP - Classification Labelling Packaging Regulation; Regulation (EC) No 1272/2008; CMR - Carcinogen, Mutagen or Reproductive Toxicant; DIN - Standard of the German Institute for Standardisation; DSL - Domestic Substances List (Canada); ECHA - European Chemicals Agency; EC-Number - European Community number; ECx - Concentration associated with x% response; ELx - Loading rate associated with x% response; EmS - Emergency Schedule; ENCS - Existing and New Chemical Substances (Japan); ErCx -
Concentration associated with x% growth rate response; GHS - Globally Harmonized System; GLP - Good Laboratory Practice; IARC - International Agency for Research on Cancer; IATA - International Air Transport Association; IBC - International Code for the Construction and Equipment of Ships carrying Dangerous Chemicals in Bulk; IC50 - Half maximal inhibitory concentration; ICAO - International Civil Aviation Organization; IECSC - Inventory of Existing Chemical Substances in China; IMDG - International Maritime Dangerous Goods; IMO - International Maritime Organization; ISHL - Industrial Safety and Health Law (Japan); ISO - International Organisation for Standardization; KECl - Korea Existing Chemicals Inventory; LC50 - Lethal Concentration to 50% of a test population; LD50 - Lethal Dose to 50% of a test population (Median Lethal Dose); MARPOL - International Convention for the Prevention of Pollution from Ships; n.o.s. - Not Otherwise Specified; NO(A)EC - No Observed (Adverse) Effect Concentration; NO(A)EL - No Observed (Adverse) Effect Level; NOELR - No Observable Effect Loading Rate; NZIoC - New Zealand Inventory of Chemicals; OECD - Organization for Economic Co-operation and Development; OPPTS - Office of Chemical Safety and Pollution Prevention; PBT - Persistent, Bioaccumulative and Toxic substance; PICCS - Philippines Inventory of Chemicals and Chemical Substances; (Q)SAR - (Quantitative) Structure Activity Relationship; REACH - Regulation (EC) No 1907/2006 of the European Parliament and of the Council concerning the Registration, Evaluation, Authorisation and Restriction of Chemicals; RID - Regulations concerning the International Carriage of Dangerous Goods by Rail; SADT - Self-Accelerating Decomposition Temperature; SDS - Safety Data Sheet; SVHC - Substance of very high concern; TCSI - Taiwan Chemical Substance Inventory; TSCA - Toxic Substances Control Act (United States); UN - United Nations; UNRTDG - United Nations Recommendations on the Transport of Dangerous Goods; vPvB - Very Persistent and Very Bioaccumulative

Further information

Classification of the mixture:
Repr. 2 H361d Calculation method
STOT RE 2 H373 Calculation method

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 is designed only as a guidance for safe handling, use, processing, storage, transportation, disposal and release and shall not be considered a warranty or quality specification of any type. The information provided relates only to the specific material identified at the top of this SDS and may not be valid when the SDS material is used in combination with any other materials or in any process, unless specified in the text. Material users should review the information and recommendations in the specific context of their intended manner of handling, use, processing and storage, including an assessment of the appropriateness of the SDS material in the user’s end product, if applicable.

NO / EN