SAFETY DATA SHEET

Rizatriptan Formulation

1. PRODUCT AND COMPANY IDENTIFICATION

Product name : Rizatriptan Formulation

Manufacturer or supplier’s details
Company : MSD
Address : Briahnager - Off Pune Nagar Road
          Wagholi - Pune - India  412 207
Telephone : 908-740-4000
Emergency telephone number : 1-908-423-6000
E-mail address : EHSDATASTEWARD@msd.com
Telefax : 908-735-1496

Recommended use of the chemical and restrictions on use
Recommended use : Pharmaceutical

2. HAZARDS IDENTIFICATION

Manufacture, Storage and Import of Hazardous Chemicals Rules 1989

Classification
Not classified as hazardous according to criteria laid down in Part I of Schedule-1.

GHS Classification
Reproductive toxicity : Category 2
Specific target organ toxicity - repeated exposure (Oral) : Category 2 (Cardio-vascular system)

GHS label elements
Hazard pictograms : !

Signal word : Warning
Hazard statements : H361d Suspected of damaging the unborn child.
                   H373 May cause damage to organs (Cardio-vascular system) through prolonged or repeated exposure if swallowed.

Precautionary statements : Prevention:
                          P201 Obtain special instructions before use.
                          P202 Do not handle until all safety precautions have been read and understood.
P260 Do not breathe dust.
P280 Wear protective gloves/ protective clothing/ eye protection/ face protection.

**Response:**
P308 + P313 IF exposed or concerned: Get medical advice/ attention.

**Storage:**
P405 Store locked up.

**Disposal:**
P501 Dispose of contents/ container to an approved waste disposal plant.

**Other hazards which do not result in classification**
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.

### 3. COMPOSITION/INFORMATION ON INGREDIENTS

<table>
<thead>
<tr>
<th>Substance / Mixture</th>
<th>Components</th>
<th>CAS-No.</th>
<th>Concentration (% w/w)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Cellulose</strong></td>
<td></td>
<td>9004-34-6</td>
<td>&gt;= 50 - &lt; 70</td>
</tr>
<tr>
<td><strong>Starch</strong></td>
<td></td>
<td>9005-25-8</td>
<td>&gt;= 10 - &lt; 20</td>
</tr>
<tr>
<td><strong>Rizatriptan</strong></td>
<td></td>
<td>145202-66-0</td>
<td>&gt;= 5 - &lt; 10</td>
</tr>
</tbody>
</table>

### 4. 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.

**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.

**Most important symptoms and effects, both acute and delayed**
Suspected of damaging the unborn child.
May cause damage to organs through prolonged or repeated exposure if swallowed.
Contact with dust can cause mechanical irritation or drying of
Dust contact with the eyes can lead to mechanical irritation. 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).

Notes to physician: Treat symptomatically and supportively.

5. FIREFIGHTING MEASURES

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

Unsuitable extinguishing media: None known.

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

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.

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

6. ACCIDENTAL RELEASE MEASURES

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

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 spills cannot be contained.

Methods and materials for containment and 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.
7. HANDLING AND STORAGE

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.

Conditions for safe storage: Keep in properly labelled containers. Store locked up. Store in accordance with the particular national regulations.

Materials to avoid: Do not store with the following product types: Strong oxidizing agents.

8. EXPOSURE CONTROLS/PERSONAL PROTECTION

Components 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>Cellulose</td>
<td>9004-34-6</td>
<td>TWA</td>
<td>10 mg/m³</td>
<td>ACGIH</td>
</tr>
<tr>
<td>Starch</td>
<td>9005-25-8</td>
<td>TWA</td>
<td>10 mg/m³</td>
<td>ACGIH</td>
</tr>
<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>

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

Respiratory protection: If adequate local exhaust ventilation is not available or exposure assessment demonstrates exposures outside the rec-
Filter type: Particulates type
Hand protection

Material: Chemical-resistant gloves

Remarks: Consider double gloving.

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.

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.

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.

9. 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.

Flammability (liquids): No data available
10. STABILITY AND REACTIVITY

Reactivity: Not classified as a reactivity hazard.
Chemical stability: Stable under normal conditions.
Possibility of hazardous reactions: May form explosive dust-air mixture during processing, handling or other means. Can react with strong oxidizing agents.

Conditions to avoid: Heat, flames and sparks. Avoid dust formation.
Incompatible materials: Oxidizing agents

11. TOXICOLOGICAL INFORMATION

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: > 5,000 mg/kg
Method: Calculation method

Components:
Cellulose:
Acute oral toxicity : LD50 (Rat): > 5,000 mg/kg
Acute inhalation toxicity : LC50 (Rat): > 5.8 mg/l
  Exposure time: 4 h
  Test atmosphere: dust/mist
Acute dermal toxicity : LD50 (Rabbit): > 2,000 mg/kg

Starch:
Acute oral toxicity : LD50 (Mouse): > 5,000 mg/kg

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 : Dermal
Species : Guinea pig
Assessment : Does not cause skin sensitisation.
Result : negative

Germ cell mutagenicity
Not classified based on available information.

Components:

Cellulose:
Genotoxicity in vitro : Test Type: Bacterial reverse mutation assay (AMES)
Result: negative

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

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:

Cellulose:
Species : Rat
Application Route : Ingestion
**Exposure time:** 72 weeks  
**Result:** negative

**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:**

**Cellulose:**
- **Effects on fertility:**  
  - **Test Type:** One-generation reproduction toxicity study  
  - **Species:** Rat  
  - **Application Route:** Ingestion  
  - **Result:** negative

- **Effects on foetal development:**  
  - **Test Type:** Fertility/early embryonic development  
  - **Species:** Rat  
  - **Application Route:** Ingestion  
  - **Result:** negative

**Rizatriptan:**
- **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 (Cardio-vascular system) through prolonged or repeated exposure if swallowed.

**Components:**

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

**Repeated dose toxicity**

**Components:**

**Cellulose:**
Species: Rat  
NOAEL: >= 9,000 mg/kg  
Application Route: Ingestion  
Exposure time: 90 Days

**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

12. ECOLOGICAL INFORMATION

Ecotoxicity

Components:

Cellulose:
Toxicity to fish : LC50 (Oryzias latipes (Japanese medaka)): > 100 mg/l
Exposure time: 48 h
Remarks: Based on data from similar materials

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 mg/l
Exposure time: 72 h
Method: OECD Test Guideline 201

Toxicity to microorganisms : EC50: > 1,000 mg/l
Exposure time: 3 h
Test Type: Respiration inhibition
Method: OECD Test Guideline 209

NOEC: 1,000 mg/l
Exposure time: 3 h
Test Type: Respiration inhibition
Method: OECD Test Guideline 209

Toxicity to fish (Chronic toxicity):

- NOEC: 9.6 mg/l
- Exposure time: 32 d
- Species: Pimephales promelas (fathead minnow)
- Method: OECD Test Guideline 210

Toxicity to daphnia and other aquatic invertebrates (Chronic toxicity):

- NOEC: 110 mg/l
- Exposure time: 21 d
- Species: Daphnia magna (Water flea)
- Method: OECD Test Guideline 211

Persistence and degradability

Components:

Cellulose:
- Biodegradability: Result: Readily biodegradable.

Rizatriptan:
- Biodegradability: Result: Not readily biodegradable.
- Biodegradation: 50%
- Exposure time: 13 d
- Method: OECD Test Guideline 314

Bioaccumulative potential

Components:

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

Mobility in soil

Components:

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

Other adverse effects

No data available

13. DISPOSAL CONSIDERATIONS

Disposal methods

- Waste from residues: Dispose of in accordance with local regulations.
- Contaminated packaging: Empty containers should be taken to an approved waste handling site for recycling or disposal. If not otherwise specified: Dispose of as unused product.
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 IMO instruments**
Not applicable for product as supplied.

15. REGULATORY INFORMATION

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

The components of this product are reported in the following inventories:

<table>
<thead>
<tr>
<th>Inventory</th>
<th>Status</th>
</tr>
</thead>
<tbody>
<tr>
<td>AICS</td>
<td>not determined</td>
</tr>
<tr>
<td>DSL</td>
<td>not determined</td>
</tr>
<tr>
<td>IECSC</td>
<td>not determined</td>
</tr>
</tbody>
</table>

16. OTHER INFORMATION

Further information


Date format: dd.mm.yyyy

Full text of other abbreviations

<table>
<thead>
<tr>
<th>Abbreviation</th>
<th>Definition</th>
</tr>
</thead>
<tbody>
<tr>
<td>ACGIH</td>
<td>USA. ACGIH Threshold Limit Values (TLV)</td>
</tr>
<tr>
<td>ACGIH / TWA</td>
<td>8-hour, time-weighted average</td>
</tr>
</tbody>
</table>

AICS - Australian Inventory of Chemical Substances; ANTT - National Agency for Transport by Land of Brazil; ASTM - American Society for the Testing of Materials; bw - Body weight; CMR - Carcinogen, Mutagen or Reproductive Toxicant; DIN - Standard of the German Institute for Standardisation; DSL - Domestic Substances List (Canada); 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; ERG - Emergency Response Guide; 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 con-
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.

IN / EN