SAFETY DATA SHEET

Rizatriptan Formulation

SECTION 1. PRODUCT AND COMPANY IDENTIFICATION

Product name: Rizatriptan Formulation

Manufacturer or supplier's details
Company: MSD
Address: Rua Treze de Maio, 1161
Campinas, São Paulo, Brazil 13106-054
Telephone: 908-740-4000
Emergency telephone: 55 19 3758 2000
E-mail address: EHSDATASETHERD@msd.com
Telefax: 908-735-1496

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

SECTION 2. HAZARDS IDENTIFICATION

GHS Classification in accordance with ABNT NBR 14725 Standard
Reproductive toxicity: Category 2
Specific target organ toxicity - repeated exposure (Oral): Category 1 (Cardio-vascular system)

GHS label elements in accordance with ABNT NBR 14725 Standard
Hazard pictograms:

Signal Word: Danger

Hazard Statements: H361d Suspected of damaging the unborn child.
H372 Causes damage to organs (Cardio-vascular system) through prolonged or repeated exposure if swallowed.

Precautionary Statements: Prevention:
P201 Obtain special instructions before use.
P260 Do not breathe dust.
P264 Wash skin thoroughly after handling.
P270 Do not eat, drink or smoke when using this product.
P280 Wear protective gloves/protective clothing/ eye protection/ face protection.

Response:
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.

SECTION 3. COMPOSITION/INFORMATION ON INGREDIENTS

<table>
<thead>
<tr>
<th>Substance / Mixture</th>
<th>Component</th>
<th>Chemical name</th>
<th>CAS-No.</th>
<th>Classification</th>
<th>Concentration (% w/w)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Cellulose</td>
<td>9004-34-6</td>
<td></td>
<td>&gt;= 50 - &lt; 70</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Starch</td>
<td>9005-25-8</td>
<td></td>
<td>&gt;= 10 - &lt; 20</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Rizatriptan</td>
<td>145202-66-0</td>
<td>Acute toxicity (Oral), Eye irritation, Category 4 Eye irritation, Category 2B Reproductive toxicity, Category 2 Specific target organ toxicity - single exposure, Category 3 Specific target organ toxicity - repeated exposure (Oral) (Cardio-vascular system), Category 1</td>
<td>&gt;= 5 - &lt; 10</td>
</tr>
</tbody>
</table>

SECTION 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 : Suspected of damaging the unborn child. Causes damage to organs through prolonged or repeated
SECTION 5. FIRE-FIGHTING MEASURES

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

Unsuitable extinguishing media : None known.

Specific hazards during fire fighting : 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 fire-fighters : In the event of fire, wear self-contained breathing apparatus. Use personal protective equipment.

SECTION 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. Sections 13 and 15 of this SDS provide information regarding certain local or national requirements.

SECTION 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.

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.

Conditions for safe storage: Keep in properly labeled 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 Organic peroxides Explosives Gases

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>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>
</tbody>
</table>
SAFETY DATA SHEET

Rizatriptan Formulation

| Rizatriptan | 145202-66-0 | TWA | 10 µg/m³ (OEB 3) | Internal Wipe limit | 100 µg/100 cm² | Internal |

**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 recommended guidelines, use respiratory protection. Particulates type

**Filter type**

**Hand protection**

**Material**: Chemical-resistant gloves

**Remarks**: Consider double gloving.

**Eye protection**: Wear safety glasses with side shields or 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.

**SECTION 9. PHYSICAL AND CHEMICAL PROPERTIES**

**Appearance**: powder

**Color**: pink

**Odor**: odorless

**Odor 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
SAFETY DATA SHEET

Rizatriptan Formulation

Flammability (solid, gas) : May form explosive dust-air mixture during processing, handling or other means.

Flammability (liquids) : No data available

Upper explosion limit / Upper flammability limit : No data available

Lower explosion limit / Lower flammability limit : No data available

Vapor pressure : No data available

Relative vapor density : No data available

Density : No data available

Solubility(ies)
Water solubility : No data available

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

Autoignition temperature : No data available

Decomposition temperature : No data available

Viscosity
Viscosity, kinematic : No data available

Explosive properties : Not explosive

Oxidizing properties : The substance or mixture is not classified as oxidizing.

Molecular weight : No data available

Particle size : No data available

SECTION 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

Hazardous decomposition products : No hazardous decomposition products are known.

SECTION 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 sensitization

Skin sensitization
Not classified based on available information.

Respiratory sensitization
Not classified based on available information.

Components:

Rizatriptan:
Test Type : Maximization Test
Routes of exposure : Dermal
Species : Guinea pig
Assessment : Does not cause skin sensitization.
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
Test Type: In vitro mammalian cell gene mutation test
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 fetal 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 fetal development:
- Test Type: Embryo-fetal development
- Species: Rat
- Application Route: Oral
- Developmental Toxicity: LOAEL: 10 mg/kg body weight
  Result: No teratogenic effects., Embryo-fetal toxicity.

  Test Type: Embryo-fetal development
  Species: Rabbit
  Application Route: Oral
  Developmental Toxicity: LOAEL: 100 mg/kg body weight
  Result: No teratogenic effects., Embryo-fetal toxicity.
  Remarks: The effects were seen only at maternally toxic dos-
es.

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:
Causes 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 y
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**

**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 fish (Chronic toxicity): NOEC (Pimephales promelas (fathead minnow)): 9,6 mg/l
   Exposure time: 32 d
   Method: OECD Test Guideline 210

Toxicity to daphnia and other aquatic invertebrates (Chronic toxicity): NOEC (Daphnia magna (Water flea)): 110 mg/l
   Exposure time: 21 d
   Method: OECD Test Guideline 211

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

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
SECTION 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.

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 for product as supplied.

国内se 規制

ANTT
Not regulated as a dangerous good

SECTION 15. REGULATORY INFORMATION

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

National List of Carcinogenic Agents for Humans - (LINACH) : Not applicable

Brazil. Ordinance No. 1274 on the control and monitoring of chemicals. : Not applicable

International Regulations

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

AICS : not determined
DSL : not determined
IECSC : not determined

SECTION 16. OTHER INFORMATION

Further information

Full text of other abbreviations:

ACGIH: USA. ACGIH Threshold Limit Values (TLV)

ACGIH / TWA: 8-hour, time-weighted average

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.

BR / Z8