Rizatriptan Formulation

1. PRODUCT AND COMPANY IDENTIFICATION

Product name : Rizatriptan Formulation

Manufacturer or supplier’s details
Company : Organon & Co.
Address : 30 Hudson Street, 33nd floor
Jersey City, New Jersey, U.S.A 07302
Telephone : 551-430-6000
Emergency telephone number : 215-631-6999
E-mail address : EHSSTEWARD@organon.com

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

2. HAZARDS IDENTIFICATION

Emergency Overview
Appearance : powder
Colour : pink
Odour : odourless
Suspected of damaging the unborn child. May cause damage to organs through prolonged or repeated exposure.

GHS Classification
Reproductive toxicity : Category 2
Specific target organ toxicity - repeated exposure : Category 2

GHS label elements
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.
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.

Physical and chemical hazards
Not classified based on available information.

Health hazards
Suspected of damaging the unborn child. May cause damage to organs through prolonged or repeated exposure.

Environmental hazards
Not classified based on available information.

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>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Chemical name</td>
</tr>
<tr>
<td></td>
<td>Cellulose</td>
</tr>
<tr>
<td></td>
<td>Starch</td>
</tr>
<tr>
<td></td>
<td>Rizatriptan</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. Contact with dust can cause mechanical irritation or drying of the skin. 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 (see section 7) and personal protective equipment recommendations (see section 8).

Environmental precautions: Avoid release to the environment. Prevent further leakage or spillage if safe to do so. Retain and dispose of contaminated wash water. Local authorities should be advised if significant spillsages 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.

7. HANDLING AND STORAGE

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. Wash skin thoroughly after handling. 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. Do not eat, drink or smoke when using this product. Take care to prevent spills, waste and minimize release to the environment.

Avoidance of contact: Oxidizing agents

Storage
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

Packaging material: Unsuitable material: None known.

8. EXPOSURE CONTROLS/PERSONAL PROTECTION

Components with workplace control parameters
Components | CAS-No. | Value type (Form of exposure) | Control parameters / Permissible concentration | Basis
--- | --- | --- | --- | ---
Cellulose | 9004-34-6 | PC-TWA | 10 mg/m³ | CN OEL
Starch | 9005-25-8 | TWA | 10 mg/m³ | ACGIH
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.

- Filter type: Particulates type
- Eye/face 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.

**Hand protection**

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

**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
### Rizatriptan Formulation

<table>
<thead>
<tr>
<th>Property</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Colour</td>
<td>pink</td>
</tr>
<tr>
<td>Odour</td>
<td>odourless</td>
</tr>
<tr>
<td>Odour Threshold</td>
<td>No data available</td>
</tr>
<tr>
<td>pH</td>
<td>No data available</td>
</tr>
<tr>
<td>Melting point/freezing point</td>
<td>No data available</td>
</tr>
<tr>
<td>Initial boiling point and boiling range</td>
<td>No data available</td>
</tr>
<tr>
<td>Flash point</td>
<td>Not applicable</td>
</tr>
<tr>
<td>Evaporation rate</td>
<td>No data available</td>
</tr>
<tr>
<td>Flammability (solid, gas)</td>
<td>May form explosive dust-air mixture during processing, handling or other means.</td>
</tr>
<tr>
<td>Flammability (liquids)</td>
<td>No data available</td>
</tr>
<tr>
<td>Upper explosion limit / Upper flammability limit</td>
<td>No data available</td>
</tr>
<tr>
<td>Lower explosion limit / Lower flammability limit</td>
<td>No data available</td>
</tr>
<tr>
<td>Vapour pressure</td>
<td>No data available</td>
</tr>
<tr>
<td>Relative vapour density</td>
<td>No data available</td>
</tr>
<tr>
<td>Density</td>
<td>No data available</td>
</tr>
<tr>
<td>Solubility(ies)</td>
<td></td>
</tr>
<tr>
<td>Water solubility</td>
<td>No data available</td>
</tr>
<tr>
<td>Partition coefficient: n-octanol/water</td>
<td>No data available</td>
</tr>
<tr>
<td>Auto-ignition temperature</td>
<td>No data available</td>
</tr>
<tr>
<td>Decomposition temperature</td>
<td>No data available</td>
</tr>
<tr>
<td>Viscosity</td>
<td></td>
</tr>
<tr>
<td>Viscosity, kinematic</td>
<td>No data available</td>
</tr>
<tr>
<td>Explosive properties</td>
<td>Not explosive</td>
</tr>
<tr>
<td>Oxidizing properties</td>
<td>The substance or mixture is not classified as oxidizing.</td>
</tr>
<tr>
<td>Molecular weight</td>
<td>No data available</td>
</tr>
</tbody>
</table>
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.

11. TOXICOLOGICAL INFORMATION

Exposure routes:
- 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 (Rat): > 5,000 mg/kg
- Acute dermal toxicity: LD50 (Rabbit): > 2,000 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:

Starch:
Species: Rabbit
Result: No eye irritation

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:

Starch:
Test Type: Maximisation Test
Exposure routes: Skin contact
Species: Guinea pig
Result: negative

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

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

Starch:

Genotoxicity in vitro

Test Type: Bacterial reverse mutation assay (AMES)
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
Rizatriptan Formulation

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

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

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

**Starch:**
Species: Rat
NOAEL: >= 2,000 mg/kg
Application Route: Skin contact
Exposure time: 28 Days
Method: OECD Test Guideline 410

**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
Rizatriptan Formulation

**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 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

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 Annex II of MARPOL 73/78 and the IBC Code
Not applicable for product as supplied.

National Regulations

GB 6944/12268
Not regulated as a dangerous good

Special precautions for user
Not applicable

15. REGULATORY INFORMATION

National regulatory information

Law on the Prevention and Control of Occupational Diseases

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

AICS : not determined

DSL : not determined

IECSC : not determined

16. OTHER INFORMATION

Further information


Date format : yyyy/mm/dd

Full text of other abbreviations

ACGIH : USA. ACGIH Threshold Limit Values (TLV)

CN OEL : Occupational exposure limits for hazardous agents in the workplace - Chemical hazardous agents.

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

CN OEL / PC-TWA : Permissible concentration - time weighted average
SAFETY DATA SHEET
according to GB/T 16483 and GB/T 17519

Rizatriptan Formulation

Version 3.9  Revision Date: 2020/10/10  SDS Number: 402485-00013  Date of last issue: 2020/03/23

Date of first issue: 2015/12/10

Disclaimer
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.

CN / EN