SAFETY DATA SHEET

Rizatriptan Orally Disintegrating Formulation

Version 2.4  Revision Date: 09.04.2021  SDS Number: 809076-00010  Date of last issue: 10.10.2020  Date of first issue: 22.07.2016

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

1.1 Product identifier
   Trade name : Rizatriptan Orally Disintegrating 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 : Organon & Co.
   30 Hudson Street, 33nd floor
   07302 Jersey City, New Jersey, U.S.A
   Telephone : 551-430-6000
   E-mail address of person responsible for the SDS : EHSSTEWARD@organon.com

1.4 Emergency telephone number
   215-631-6999

SECTION 2: Hazards identification

2.1 Classification of the substance or mixture
   Classification (REGULATION (EC) No 1272/2008)
   Skin sensitisation, Category 1 : H317: May cause an allergic skin reaction.
   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 : H317 May cause an allergic skin reaction.
   H373 May cause damage to organs through prolonged or repeated exposure.
   Precautionary statements : Prevention:
   P260 Do not breathe dust.
   P272 Contaminated work clothing should not be allowed out of the workplace.
   P280 Wear protective gloves.
Response:
P314 Get medical advice/attention if you feel unwell.
P333 + P313 If skin irritation or rash occurs: Get medical advice/attention.
P362 + P364 Take off contaminated clothing and wash it before reuse.

Hazardous components which must be listed on the label:
Peppermint oil
Rizatriptan

2.3 Other hazards
This substance/mixture contains no components considered to be either persistent, bioaccumulative and toxic (PBT), or very persistent and very bioaccumulative (vPvB) at levels of 0.1% or higher.
Dust contact with the eyes can lead to mechanical irritation.
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>Classification</th>
<th>Concentration (% w/w)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Peppermint oil</td>
<td>8006-90-4</td>
<td></td>
<td></td>
<td>Skin Irrit. 2; H315 Eye Irrit. 2; H319 Skin Sens. 1; H317 Aquatic Chronic 3; H412</td>
<td>&gt;= 2.5 - &lt; 10</td>
</tr>
<tr>
<td>Rizatriptan</td>
<td>145202-66-0</td>
<td></td>
<td></td>
<td>Acute Tox. 4; H302 Eye Irrit. 2; H319 Repr. 2; H361d STOT SE 3; H336 STOT RE 1; H372 (Cardio-vascular system)</td>
<td>&gt;= 1 - &lt; 3</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 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:
- May cause an allergic skin reaction.
- May cause damage to organs through prolonged or repeated exposure.
- 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
- Nitrogen oxides (NOx)

5.3 Advice for firefighters

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

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 (see section 7) and personal protective equipment recommendations (see section 8).

6.2 Environmental precautions

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 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 get on skin or clothing.
- Do not breathe dust.
Do not swallow.
Avoid contact with eyes.
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.

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. Contaminated work clothing should not be allowed out of the workplace. 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 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 Exposure limits

<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>Cellulose</td>
<td>9004-34-6</td>
<td>TWA OEL-RL (Respirable dust)</td>
<td>5 mg/m3</td>
<td>ZA OEL</td>
</tr>
</tbody>
</table>
| Further information: Recommended Limit

| Further information: Recommended Limit
| TWA OEL-RL (inhaled dust) | 10 mg/m3 | ZA OEL |

| Further information: Recommended Limit
| STEL OEL-RL (Dust) | 20 mg/m3 | ZA OEL |

Further information: Recommended Limit
Starch | 9005-25-8 | TWA OEL-RL (Respirable dust) | 5 mg/m3 | ZA OEL
Further information: Recommended Limit
--- | --- | --- | --- | ---
 |  | TWA OEL-RL (inhalable dust) | 10 mg/m3 | ZA OEL
Further information: Recommended Limit
Rizatriptan | 145202-66-0 | TWA | 10 µg/m3 (OEB 3) | Internal
 |  | Wipe limit | 100 µg/100 cm² | Internal

### 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**: No data available
- **Odour**: No data available
- **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
Relative density: No data available
Density: No data available
Solubility(ies)
Water solubility: No data available
Partition coefficient: n-octanol/water: No data available
Auto-ignition 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.

9.2 Other information
Flammability (liquids): No data available
Molecular weight: No data available
Particle size: 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:

Peppermint oil:
Acute oral toxicity: LD50 (Rat): > 2.000 mg/kg
Acute dermal toxicity: LD50 (Rabbit): > 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:

Peppermint oil:
Species: Rabbit
Result: Skin irritation
Remarks: Based on data from similar materials
## Rizatriptan

### Species:
- Rabbit

### Result:
- No skin irritation

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

### Components:

#### Peppermint oil:
- **Species:** Rabbit
- **Result:** Irritation to eyes, reversing within 21 days
- **Remarks:** Based on data from similar materials

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

### Respiratory or skin sensitisation

#### Skin sensitisation
May cause an allergic skin reaction.

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

### Components:

#### Peppermint oil:
- **Test Type:** Local lymph node assay (LLNA)
- **Exposure routes:** Skin contact
- **Species:** Mouse
- **Method:** OECD Test Guideline 429
- **Result:** positive
- **Remarks:** Based on data from similar materials

- **Assessment:** Probability or evidence of skin sensitisation in humans

#### 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:

#### 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
Not classified based on available information.

**Components:**

**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 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
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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:

Peppermint oil:
Toxicity to fish : LL50 (Danio rerio (zebra fish)) : > 10 - 100 mg/l
Exposure time: 96 h
Remarks: Based on data from similar materials

Toxicity to daphnia and other aquatic invertebrates : EL50 (Daphnia magna (Water flea)) : > 10 - 100 mg/l
Exposure time: 48 h
Remarks: Based on data from similar materials

Toxicity to algae/aquatic plants : EL50 (Desmodesmus subspicatus (green algae)) : > 10 - 100 mg/l
Exposure time: 72 h
Remarks: Based on data from similar materials

Toxicity to microorganisms : EC10 : 51 mg/l
Exposure time: 3 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
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

12.2 Persistence and degradability

Components:

Peppermint oil:
Biodegradability: Result: Readily biodegradable.
Remarks: Based on data from similar materials

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

12.3 Bioaccumulative potential

Components:

Peppermint oil:
Partition coefficient: n-octanol/water: log Pow: > 4
Remarks: Based on data from similar materials

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

Product:
Assessment: This substance/mixture contains no components considered to be either persistent, bioaccumulative and toxic (PBT), or very persistent and very bioaccumulative (vPvB) at levels of 0.1% or higher.

12.6 Other adverse effects

Product:
Endocrine disrupting potential: The substance/mixture does not contain components considered to have endocrine disrupting properties according to REACH Article 57(f) or Commission Delegated regulation (EU) 2017/2100 or Commission Regulation (EU) 2018/605 at levels of 0.1% or higher.

SECTION 13: Disposal considerations

13.1 Waste treatment methods

Product: 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.

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

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

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.
- H315: Causes skin irritation.
- H317: May cause an allergic skin reaction.
- 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.
- H412: Harmful to aquatic life with long lasting effects.

Full text of other abbreviations

- Acute Tox.: Acute toxicity
- Aquatic Chronic: Long-term (chronic) aquatic hazard
- Eye Irrit.: Eye irritation
- Repr.: Reproductive toxicity
- Skin Irrit.: Skin irritation
- Skin Sens.: Skin sensitisation
- STOT RE: Specific target organ toxicity - repeated exposure
- STOT SE: Specific target organ toxicity - single exposure
- ZA OEL: South Africa. Hazardous Chemical Substances Regulations, Occupational Exposure Limits
- ZA OEL / TWA OEL-RL: Long term occupational exposure limits - recommended limit
- ZA OEL / STEL OEL-RL: Short term occupational exposure limits - recommended limit

ADN - European Agreement concerning the International Carriage of Dangerous Goods by Inland Waterways; ADR - European Agreement concerning the International Carriage of Dangerous
Further information

Sources of key data used to compile the Safety Data Sheet:

Classification of the mixture:
Skin Sens. 1: H317
STOT RE 2: H373

Classification procedure:
Calculation method
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.

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