1. PRODUCT AND COMPANY IDENTIFICATION

Product name: Rizatriptan Orally Disintegrating Formulation

Manufacturer or supplier’s details
Company: MSD
Address: 50 Tuas West Drive
          Singapore - Singapore 638408
Telephone: 908-740-4000
Emergency telephone number: 65 6697 2111 (24/7/365)
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

GHS Classification
Skin sensitisation: Category 1
Specific target organ toxicity - repeated exposure (Oral): Category 2 (Cardio-vascular system)

GHS label elements
Hazard pictograms:
Signal word: Warning
Hazard statements: H317 May cause an allergic skin reaction. H373 May cause damage to organs (Cardio-vascular system) through prolonged or repeated exposure if swallowed.

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:
P302 + P352 IF ON SKIN: Wash with plenty of water.
P314 Get medical advice/ attention if you feel unwell.
P333 + P313 If skin irritation or rash occurs: Get medical ad-
SAFETY DATA SHEET

Rizatriptan Orally Disintegrating Formulation

Version 1.7  Revision Date: 09/13/2019  SDS Number: 809074-00008  Date of last issue: 24.04.2019

vice/ attention.
P362 + P364 Take off contaminated clothing and wash it before reuse.

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.
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>Mixture</td>
<td>Cellulose</td>
</tr>
<tr>
<td></td>
<td>Peppermint oil</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 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:
May cause an allergic skin reaction.
May cause damage to organs through prolonged or repeated exposure if swallowed.
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
SAFETY DATA SHEET

Rizatriptan Orally Disintegrating Formulation

Version: 1.7
Revision Date: 09/13/2019
SDS Number: 809074-00008
Date of last issue: 24.04.2019
Date of first issue: 22.07.2016

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, Nitrogen oxides (NOx)
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 spillages 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

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.
SAFETY DATA SHEET

Rizatriptan Orally Disintegrating Formulation

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.
- 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 in accordance with the particular national regulations.

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

8. EXPOSURE CONTROLS/PERSOAL 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>PEL (long term)</td>
<td>10 mg/m3</td>
<td>SG OEL</td>
</tr>
<tr>
<td></td>
<td></td>
<td>TWA</td>
<td>10 mg/m3</td>
<td>ACGIH</td>
</tr>
<tr>
<td>Starch</td>
<td>9005-25-8</td>
<td>PEL (long term)</td>
<td>10 mg/m3</td>
<td>SG OEL</td>
</tr>
<tr>
<td></td>
<td></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</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 recommended guidelines, use respiratory protection.
- Filter type: Particulates type
- Hand protection: 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: 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.

Flammability (liquids): No data available

Upper explosion limit / Upper flammability limit: No data available

Lower explosion limit / Lower flammability limit: 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
Hazardous decomposition products: No hazardous decomposition products are known.

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: > 2,000 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

Peppermint oil:
Acute oral toxicity: LD50 (Rat): > 2,000 mg/kg
Acute dermal toxicity: LD50 (Rabbit): > 5,000 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:

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: Eye irritation
Remarks: Based on data from similar materials
Rizatriptan Orally Disintegrating Formulation

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:

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

Genotoxicity in vivo : Test Type: In vitro mammalian cell gene mutation test
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  
Not classified based on available information.  

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: $\geq 9,000$ 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

Peppermint oil:
<p>| | | |</p>
<table>
<thead>
<tr>
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</thead>
<tbody>
<tr>
<td><strong>Toxicity to fish</strong></td>
<td><strong>LL50 (Danio rerio (zebra fish)): &gt; 10 - 100 mg/l</strong></td>
<td></td>
</tr>
<tr>
<td></td>
<td><strong>Exposure time: 96 h</strong></td>
<td><strong>Remarks: Based on data from similar materials</strong></td>
</tr>
<tr>
<td><strong>Toxicity to daphnia and other aquatic invertebrates</strong></td>
<td><strong>EL50 (Daphnia magna (Water flea)): &gt; 10 - 100 mg/l</strong></td>
<td></td>
</tr>
<tr>
<td></td>
<td><strong>Exposure time: 48 h</strong></td>
<td><strong>Remarks: Based on data from similar materials</strong></td>
</tr>
<tr>
<td><strong>Toxicity to algae/aquatic plants</strong></td>
<td><strong>EL50 (Desmodesmus subspicatus (green algae)): &gt; 10 - 100 mg/l</strong></td>
<td></td>
</tr>
<tr>
<td></td>
<td><strong>Exposure time: 72 h</strong></td>
<td><strong>Remarks: Based on data from similar materials</strong></td>
</tr>
<tr>
<td><strong>Toxicity to microorganisms</strong></td>
<td><strong>EC10: 51 mg/l</strong></td>
<td></td>
</tr>
<tr>
<td></td>
<td><strong>Exposure time: 3 h</strong></td>
<td><strong>Remarks: Based on data from similar materials</strong></td>
</tr>
</tbody>
</table>

**Rizatriptan:**

<p>| | | |</p>
<table>
<thead>
<tr>
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</thead>
<tbody>
<tr>
<td><strong>Toxicity to fish</strong></td>
<td><strong>LC50 (Pimephales promelas (fathead minnow)): &gt; 1,000 mg/l</strong></td>
<td></td>
</tr>
<tr>
<td></td>
<td><strong>Exposure time: 96 h</strong></td>
<td><strong>Remarks: Based on data from similar materials</strong></td>
</tr>
<tr>
<td><strong>Toxicity to daphnia and other aquatic invertebrates</strong></td>
<td><strong>EC50 (Daphnia magna (Water flea)): 1,000 mg/l</strong></td>
<td></td>
</tr>
<tr>
<td></td>
<td><strong>Exposure time: 48 h</strong></td>
<td></td>
</tr>
<tr>
<td><strong>Toxicity to algae/aquatic plants</strong></td>
<td><strong>EC50 (Pseudokirchneriella subcapitata (green algae)): &gt; 100 mg/l</strong></td>
<td></td>
</tr>
<tr>
<td></td>
<td><strong>Exposure time: 72 h</strong></td>
<td><strong>Method: OECD Test Guideline 201</strong></td>
</tr>
<tr>
<td></td>
<td></td>
<td><strong>NOEC (Pseudokirchneriella subcapitata (green algae)): 48 mg/l</strong></td>
</tr>
<tr>
<td></td>
<td></td>
<td><strong>Exposure time: 72 h</strong></td>
</tr>
<tr>
<td><strong>Toxicity to fish (Chronic toxicity)</strong></td>
<td><strong>NOEC (Pimephales promelas (fathead minnow)): 9.6 mg/l</strong></td>
<td></td>
</tr>
<tr>
<td></td>
<td><strong>Exposure time: 32 d</strong></td>
<td><strong>Method: OECD Test Guideline 210</strong></td>
</tr>
<tr>
<td><strong>Toxicity to daphnia and other aquatic invertebrates (Chronic toxicity)</strong></td>
<td><strong>NOEC (Daphnia magna (Water flea)): 110 mg/l</strong></td>
<td></td>
</tr>
<tr>
<td></td>
<td><strong>Exposure time: 21 d</strong></td>
<td><strong>Method: OECD Test Guideline 211</strong></td>
</tr>
<tr>
<td><strong>Toxicity to microorganisms</strong></td>
<td><strong>EC50: &gt; 1,000 mg/l</strong></td>
<td></td>
</tr>
<tr>
<td></td>
<td><strong>Exposure time: 3 h</strong></td>
<td><strong>Test Type: Respiration inhibition</strong></td>
</tr>
<tr>
<td></td>
<td></td>
<td><strong>Method: OECD Test Guideline 209</strong></td>
</tr>
<tr>
<td></td>
<td></td>
<td><strong>NOEC: 1,000 mg/l</strong></td>
</tr>
<tr>
<td></td>
<td></td>
<td><strong>Exposure time: 3 h</strong></td>
</tr>
<tr>
<td></td>
<td></td>
<td><strong>Test Type: Respiration inhibition</strong></td>
</tr>
<tr>
<td></td>
<td></td>
<td><strong>Method: OECD Test Guideline 209</strong></td>
</tr>
</tbody>
</table>
Persistence and degradability

**Components:**

**Cellulose:**
Biodegradability: Result: Readily biodegradable.

**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

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

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
SAFETY DATA SHEET
Rizatriptan Orally Disintegrating Formulation

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.

15. REGULATORY INFORMATION

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

Workplace Safety and Health Act and Workplace Safety and Health (General Provisions) Regulations: This product is subjected to the SDS, labelling, PEL and other requirements in the Act/Regulations.

Environmental Protection and Management Act and Environmental Protection and Management (Hazardous Substances) Regulations: Not applicable

Fire Safety (Petroleum and Flammable Materials) Regulations: Not applicable

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 : dd.mm.yyyy

Full text of other abbreviations
ACGIH : USA. ACGIH Threshold Limit Values (TLV)
SG OEL : Singapore. Workplace Safety and Health Act - First Schedule Permissible Exposure Limits of Toxic Substances

ACGIH / TWA : 8-hour, time-weighted average
SG OEL / PEL (long term) : Permissible Exposure Level (PEL) Long Term
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.