SAFETY DATA SHEET

Rizatriptan Orally Disintegrating Formulation

Version 1.9  Revision Date: 2020/10/10  SDS Number: 809066-00010  Date of last issue: 2020/03/23
Date of first issue: 2016/07/22

1. PRODUCT AND COMPANY IDENTIFICATION

Product name: Rizatriptan Orally Disintegrating Formulation

Manufacturer or supplier’s details
Company: MSD
Address: JL Raya Pandaan KM. 48
Pandaan, Jawa Timur - Indonesia
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

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-
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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

Substance / Mixture : Mixture

Components

<table>
<thead>
<tr>
<th>Chemical name</th>
<th>CAS-No.</th>
<th>Concentration (% w/w)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cellulose</td>
<td>9004-34-6</td>
<td>&gt;= 10 - &lt; 30</td>
</tr>
<tr>
<td>Peppermint oil</td>
<td>8006-90-4</td>
<td>&gt;= 2.5 - &lt; 10</td>
</tr>
<tr>
<td>Starch</td>
<td>9005-25-8</td>
<td>&lt; 10</td>
</tr>
<tr>
<td>Rizatriptan</td>
<td>145202-66-0</td>
<td>&gt;= 1 - &lt; 3</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
3. Dangerous properties

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
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 (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 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.
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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.

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/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>Peppermint oil</td>
<td>8006-90-4</td>
<td>NAB (Mist)</td>
<td>10 mg/m³</td>
<td>ID OEL</td>
</tr>
<tr>
<td>Starch</td>
<td>9005-25-8</td>
<td>NAB</td>
<td>10 mg/m³</td>
<td>ID OEL</td>
</tr>
</tbody>
</table>

Further information: Adopted in Year 1996, Not classified as carcinogenic to humans. Not enough data to classify these materials as carcinogenic to humans or animals.

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<th>Basis</th>
</tr>
</thead>
<tbody>
<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 recommended guidelines, use respiratory protection.
  - Filter type
  - Hand protection

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</table>

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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. 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.

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 : 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 (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:**

**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

Starch:
Species: Rabbit
Result: No eye irritation

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

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

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 dos-
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

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
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:
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: EC50 (Daphnia magna (Water flea)): 1,000 mg/l
aquatic invertebrates: 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.

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- log Pow: > 4
octanol/water

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

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

Minister of Industry Regulation No. 23/M-IND/PER/4/2013 concerning the Revision of Minister of Industry Regulation No. 87/M-IND/PER/9/2009 concerning Globally Harmonized System of Classification and Labelling of Chemicals.

Regulation of the Minister of Health No. 472 of 1996 on the Safeguarding of Substances Hazardous to Health
Hazardous substances that must be registered
: Not applicable
Government Regulation No. 74 of 2001 on the Management of Hazardous and Toxic Substances
Hazardous substances approved for use : Not applicable
Prohibited substances : Not applicable
Restricted substances : Not applicable

Regulation of the Minister of Trade No. 44 of 2009 on Procurement, Distribution and Supervision of Hazardous Materials
Type of Hazardous Materials Restricted to Import, Distribution and Supervision : 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 : yyyy/mm/dd

Full text of other abbreviations
ACGIH : USA. ACGIH Threshold Limit Values (TLV)
ID OEL : Indonesia. Occupational Exposure Limits

AICIC - Australian Inventory of Industrial Chemicals; 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 concentration; ICAO - International Civil Aviation Organization; IECSC - Inventory of Existing Chemical Substances in China; IMDG - International Maritime Dangerous Goods; IMO - International Maritime Organization; ISHL - Industrial Safety and Health Law (Japan); ISO - International Or-
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.