SAFETY DATA SHEET

Atorvastatin Formulation

SECTION 1. PRODUCT AND COMPANY IDENTIFICATION

Product name : Atorvastatin Formulation

Manufacturer or supplier’s details

Company : MSD
Address : 855 Leandro N. Alem St., 8 Floor
Buenos Aires, Argentina C1001AFB
Telephone : 908-740-4000
Emergency telephone : 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

SECTION 2. HAZARDS IDENTIFICATION

GHS Classification

Specific target organ toxicity - repeated exposure (Oral) : Category 2 (Liver, muscle)
Long-term (chronic) aquatic hazard : Category 3

GHS label elements

Hazard pictograms :

Signal Word : Warning
Hazard Statements : H373 May cause damage to organs (Liver, muscle) through prolonged or repeated exposure if swallowed. H412 Harmful to aquatic life with long lasting effects.
Precautionary Statements :

Prevention:
P260 Do not breathe dust.
P273 Avoid release to the environment.

Response:
P314 Get medical advice/ attention if you feel unwell.

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.
Contact with dust can cause mechanical irritation or drying of the skin.
May form explosive dust-air mixture during processing, handling or other means.

### SECTION 3. COMPOSITION/INFORMATION ON INGREDIENTS

<table>
<thead>
<tr>
<th>Substance / Mixture</th>
<th>Components</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mixture</td>
<td></td>
</tr>
</tbody>
</table>

<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;= 20 -&lt; 30</td>
</tr>
<tr>
<td>Atorvastatin</td>
<td>134523-03-8</td>
<td>&gt;= 10 -&lt; 20</td>
</tr>
</tbody>
</table>

### SECTION 4. FIRST AID MEASURES

**General advice:** In the case of accident or if you feel unwell, seek medical advice immediately.
When symptoms persist or in all cases of doubt seek medical advice.

**If inhaled:** If inhaled, remove to fresh air.
Get medical attention if symptoms occur.

**In case of skin contact:** Wash with water and soap.
Get medical attention if symptoms occur.

**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 if symptoms occur.
Rinse mouth thoroughly with water.

**Most important symptoms and effects, both acute and delayed:** May cause damage to organs through prolonged or repeated exposure if swallowed.
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.

### SECTION 5. FIRE-FIGHTING MEASURES

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

**Unsuitable extinguishing media:** None known.

**Specific hazards during fire fighting:** Avoid generating dust; fine dust dispersed in air in sufficient concentrations, and in the presence of an ignition source is a potential dust explosion hazard.
Exposure to combustion products may be a hazard to health.

Hazardous combustion products:
- Carbon oxides
- Nitrogen oxides (NOx)
- Fluorine compounds
- Metal oxides

Specific extinguishing methods:
- Use extinguishing measures that are appropriate to local circumstances and the surrounding environment.
- Use water spray to cool unopened containers.
- Remove undamaged containers from fire area if it is safe to do so.
- Evacuate area.

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

SECTION 6. ACCIDENTAL RELEASE MEASURES

Personal precautions, protective equipment and emergency procedures:
- Use personal protective equipment.
- Follow safe handling advice and personal protective equipment recommendations.

Environmental precautions:
- Discharge into the environment must be avoided.
- Prevent further leakage or spillage if safe to do so.
- Retain and dispose of contaminated wash water.
- Local authorities should be advised if significant 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.

SECTION 7. HANDLING AND STORAGE

Technical measures:
- Static electricity may accumulate and ignite suspended dust causing an explosion.
- Provide adequate precautions, such as electrical grounding and bonding, or inert atmospheres.

Local/Total ventilation:
- Use only with adequate ventilation.

Advice on safe handling:
- Do not breathe dust.
- Do not swallow.
- Avoid contact with eyes.
- Avoid prolonged or repeated contact with skin.
- Handle in accordance with good industrial hygiene and safety.
practice, based on the results of the workplace exposure assessment.
Minimize dust generation and accumulation.
Keep container closed when not in use.
Keep away from heat and sources of ignition.
Take precautionary measures against static discharges.
Take care to prevent spills, waste and minimize release to the environment.

Conditions for safe storage:
- Keep in properly labeled containers.
- Store in accordance with the particular national regulations.

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

SECTION 8. EXPOSURE CONTROLS/PERSONAL PROTECTION

Ingredients with workplace control parameters

<table>
<thead>
<tr>
<th>Components</th>
<th>CAS-No.</th>
<th>Value type (Form of exposure)</th>
<th>Control parameters / Permissible concentration</th>
<th>Basis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cellulose</td>
<td>9004-34-6</td>
<td>CMP</td>
<td>10 mg/m³</td>
<td>AR OEL</td>
</tr>
<tr>
<td></td>
<td></td>
<td>TWA</td>
<td>10 mg/m³</td>
<td>ACGIH</td>
</tr>
<tr>
<td>Atorvastatin</td>
<td>134523-03-8</td>
<td>TWA</td>
<td>0.05 mg/m³ (OEB 3)</td>
<td>Internal</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Wipe limit</td>
<td>0.5 mg/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

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
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.

SECTION 9. PHYSICAL AND CHEMICAL PROPERTIES

Appearance: granular

Color: No data available

Odor: No data available

Odor Threshold: No data available

pH: No data available

Melting point/freezing point: No data available

Initial boiling point and boiling range: No data available

Flash point: No data available

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

Vapor pressure: No data available

Relative vapor density: No data available

Density: No data available

Solubility(ies)
  Water solubility: No data available
SECTION 10. STABILITY AND REACTIVITY

Reactivity: Not classified as a reactivity hazard.
Chemical stability: Stable under normal conditions.
Possibility of hazardous reactions: May form explosive dust-air mixture during processing, handling or other means. Can react with strong oxidizing agents.

Conditions to avoid: Heat, flames and sparks. Avoid dust formation.
Incompatible materials: Oxidizing agents
Hazardous decomposition products: No hazardous decomposition products are known.

SECTION 11. TOXICOLOGICAL INFORMATION

Information on likely routes of exposure: Inhalation, Skin contact, Ingestion, Eye contact

Acute toxicity: Not classified based on available information.

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

Atorvastatin:
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Acute oral toxicity:
LD50 (Rat, male and female): > 5.000 mg/kg
LD50 (Mouse, male and female): > 5.000 mg/kg

Skin corrosion/irritation
Not classified based on available information.

**Components:**

**Atorvastatin:**
Species: Rabbit
Result: No skin irritation

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

**Components:**

**Atorvastatin:**
Species: Rabbit
Result: No eye irritation
Method: Draize Test

Respiratory or skin sensitization

Skin sensitization
Not classified based on available information.

Respiratory sensitization
Not classified based on available information.

**Components:**

**Atorvastatin:**
Test Type: Maximization Test
Routes of exposure: Skin contact
Species: Guinea pig
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

Atorvastatin:

Genotoxicity in vitro:
- Test Type: reverse mutation assay  
  Test system: Salmonella typhimurium  
  Result: negative
- Test Type: reverse mutation assay  
  Test system: Escherichia coli  
  Result: negative
- Test Type: In vitro mammalian cell gene mutation test  
  Test system: Chinese hamster lung cells  
  Result: negative
- Test Type: sister chromatid exchange assay  
  Test system: Chinese hamster lung cells  
  Result: negative

Genotoxicity in vivo:
- Test Type: In vivo micronucleus test  
  Species: Mouse  
  Cell type: Bone marrow  
  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

Atorvastatin:
- Species: Mouse, male and female  
  Application Route: oral (gavage)  
  Exposure time: 2 Years  
  NOAEL: 200 mg/kg body weight  
  LOAEL: 400 mg/kg body weight  
  Result: negative  
  Target Organs: Liver
- Species: Rat, female  
  Application Route: oral (gavage)  
  Exposure time: 2 Years  
  LOAEL: 100 mg/kg body weight  
  Target Organs: Musculo-skeletal system
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 fetal development
Test Type: Fertility/early embryonic development
Species: Rat
Application Route: Ingestion
Result: negative

Atorvastatin:
Effects on fertility
Test Type: Fertility/early embryonic development
Species: Rat, female
Fertility: NOAEL: 225 mg/kg body weight
Result: No effects on fertility.

Test Type: Fertility/early embryonic development
Species: Rat, male
Fertility: NOAEL: 175 mg/kg body weight
Result: No effects on fertility.

Effects on fetal development
Species: Rat, female
Developmental Toxicity: NOAEL: 20 mg/kg body weight
Result: No teratogenic effects., Embryo-fetal toxicity.
Remarks: Maternal toxicity observed.

Species: Rabbit, female
Application Route: Oral
Developmental Toxicity: NOAEL: 100 mg/kg body weight
Result: No embryo-fetal toxicity.

STOT-single exposure
Not classified based on available information.

STOT-repeated exposure
May cause damage to organs (Liver, muscle) through prolonged or repeated exposure if swallowed.

Components:

Atorvastatin:
Routes of exposure: Ingestion
Target Organs: Liver, muscle
Assessment: May cause 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

**Atorvastatin:**
Species: Rat, male and female
LOAEL: 70 mg/kg
Application Route: oral (gavage)
Exposure time: 52 Weeks
Target Organs: Liver

Species: Dog
LOAEL: 10 mg/kg
Application Route: oral (gavage)
Exposure time: 104 Weeks
Target Organs: Liver

Aspiration toxicity
Not classified based on available information.

Experience with human exposure

**Components:**

**Atorvastatin:**
Ingestion: Symptoms: muscle pain, Fatigue, stomach discomfort, Abdominal pain, constipation, flatulence, liver function change

SECTION 12. ECOLOGICAL INFORMATION

Ecotoxicity

**Components:**

**Cellulose:**
Toxicity to fish: LC50 (Oryzias latipes (Japanese medaka)): > 100 mg/l
Exposure time: 48 h
Remarks: Based on data from similar materials

**Atorvastatin:**
Toxicity to fish: LC50 (Pimephales promelas (fathead minnow)): > 92 mg/l
Exposure time: 96 h
Method: OECD Test Guideline 203

Toxicity to daphnia and other aquatic invertebrates: EC50 (Daphnia magna (Water flea)): 200 mg/l
Exposure time: 48 h
Method: OECD Test Guideline 202
Toxicity to algae/aquatic plants:
EC50 (Pseudokirchneriella subcapitata (green algae)): 108 mg/l
Exposure time: 72 h
Method: OECD Test Guideline 201

NOEC (Pseudokirchneriella subcapitata (green algae)): 14 mg/l
Exposure time: 72 h
Method: OECD Test Guideline 201

Toxicity to fish (Chronic toxicity):
NOEC (Pimephales promelas (fathead minnow)): 0.49 mg/l
Exposure time: 33 d
Method: OECD Test Guideline 210

Toxicity to daphnia and other aquatic invertebrates (Chronic toxicity):
NOEC (Daphnia magna (Water flea)): 0.2 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

Persistence and degradability

Components:

Cellulose:
Biodegradability: Result: Readily biodegradable.

Atorvastatin:
Biodegradability: Result: Not readily biodegradable.
Biodegradation: 7.7 %
Exposure time: 28 d
Method: OECD Test Guideline 314

Bioaccumulative potential

Components:

Atorvastatin:
Partition coefficient: n-octanol/water: log Pow: 1.62

Mobility in soil

Components:

Atorvastatin:
Distribution among environmental compartments: log Koc: 2.84

Other adverse effects
No data available
SECTION 13. DISPOSAL CONSIDERATIONS

Disposal methods
- Waste from residues: Dispose of in accordance with local regulations.
- Contaminated packaging: Empty containers should be taken to an approved waste handling site for recycling or disposal. If not otherwise specified: Dispose of as unused product.

SECTION 14. TRANSPORT INFORMATION

International Regulations
- UNRTDG: Not regulated as a dangerous good
- IATA-DGR: Not regulated as a dangerous good
- IMDG-Code: Not regulated as a dangerous good

Transport in bulk according to Annex II of MARPOL 73/78 and the IBC Code
Not applicable for product as supplied.

SECTION 15. REGULATORY INFORMATION

Safety, health and environmental regulations/legislation specific for the substance or mixture
- Argentina. Carcinogenic Substances and Agents Registry: Not applicable
- Control of precursors and essential chemicals for the preparation of drugs: Not applicable

International Regulations
The ingredients of this product are reported in the following inventories:
- AICS: not determined
- DSL: not determined
- IECSC: not determined

SECTION 16. OTHER INFORMATION

Further information

Full text of other abbreviations
SAFETY DATA SHEET

Atorvastatin Formulation

Version 3.3  Revision Date: 23.03.2020  SDS Number: 187327-00010  Date of last issue: 13.09.2019
Date of first issue: 17.06.2015

ACGIH : USA. ACGIH Threshold Limit Values (TLV)
AR OEL : Argentina. Occupational Exposure Limits

ACGIH / TWA : 8-hour, time-weighted average
AR OEL / CMP : TLV (Threshold Limit Value)

AICS - Australian Inventory of Chemical Substances; 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 Organisation for Standardisation; KECI - Korea Existing Chemicals Inventory; LC50 - Lethal Concentration to 50 % of a test population; LD50 - Lethal Dose to 50% of a test population (Median Lethal Dose); MARPOL - International Convention for the Prevention of Pollution from Ships; n.o.s. - Not Otherwise Specified; Nch - Chilean Norm; NO(A)EC - No Observed (Adverse) Effect Concentration; NO(A)EL - No Observed (Adverse) Effect Level; NOELR - No Observable Effect Loading Rate; NOM - Official Mexican Norm; NTP - National Toxicology Program; NZIoC - New Zealand Inventory of Chemicals; OECD - Organization for Economic Co-operation and Development; OPPTS - Office of Chemical Safety and Pollution Prevention; PBT - Persistent, Bioaccumulative and Toxic substance; PICCS - Philippines Inventory of Chemicals and Chemical Substances; (Q)SAR - (Quantitative) Structure Activity Relationship; REACH - Regulation (EC) No 1907/2006 of the European Parliament and of the Council concerning the Registration, Evaluation, Authorisation and Restriction of Chemicals; SADT - Self-Accelerating Decomposition Temperature; SDS - Safety Data Sheet; TCSI - Taiwan Chemical Substance Inventory; TDG - Transportation of Dangerous Goods; TSCA - Toxic Substances Control Act (United States); UN - United Nations; UNRTOG - United Nations Recommendations on the Transport of Dangerous Goods; vPvB - Very Persistent and Very Bioaccumulative; WHMIS - Workplace Hazardous Materials Information System

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.

AR / Z8