SAFETY DATA SHEET

Atorvastatin Formulation

SECTION 1. PRODUCT AND COMPANY IDENTIFICATION

Product name : Atorvastatin Formulation

Manufacturer or supplier's details
Company : MSD
Address : Rua Treze de Maio, 1161
Campinas, São Paulo, Brazil 13106-054
Telephone : 908-740-4000
Emergency telephone : 55 19 3758 2000
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 in accordance with ABNT NBR 14725 Standard
Specific target organ toxicity - repeated exposure (Oral) : Category 2 (Liver, muscle)
Long-term (chronic) aquatic hazard : Category 3

GHS label elements in accordance with ABNT NBR 14725 Standard
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.
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>
<th>Chemical name</th>
<th>CAS-No.</th>
<th>Classification</th>
<th>Concentration (% w/w)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mixture</td>
<td>Cellulose</td>
<td>9004-34-6</td>
<td>Specific target organ toxicity - repeated exposure (Oral) (Liver, muscle), Category 2 Long-term (chronic) aquatic hazard, Category 2</td>
<td>&gt;= 20 -&lt; 30</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Atorvastatin</td>
<td>134523-03-8</td>
<td></td>
<td>&gt;= 10 -&lt; 20</td>
<td></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: None known.
media
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: 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 (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.

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.  

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.  

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>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  
Hand protection : Particulates type
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.

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
SAFETY DATA SHEET
Atorvastatin Formulation

Solubility(ies)
- Water solubility: No data available
- Partition coefficient: n-octanol/water: No data available
- Autoignition 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.

Molecular weight
- No data available

Particle size
- 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
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Atorvastatin:
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

**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.

**Domestic regulation**

**ANTT**
- Not regulated as a dangerous good

SECTION 15. REGULATORY INFORMATION

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

**National List of Carcinogenic Agents for Humans - (LINACH)**
- Not applicable

**Brazil. List of chemicals controlled by the Federal Police**
- Calcium carbonate

**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**

Sources of key data used to: Internal technical data, data from raw material SDSs, OECD

Full text of other abbreviations

ACGIH : USA. ACGIH Threshold Limit Values (TLV)

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

AILC - 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 Organisation for Standardization; 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; UNRTDG - 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.

BR / Z8