Atorvastatin Formulation

1. PRODUCT AND COMPANY IDENTIFICATION

Product name: Atorvastatin Formulation

Manufacturer or supplier's details
Company: MSD
Address: 199 Wenhai North Road, HEDA, Hangzhou - Zhejiang Province - CHINA 310018
Telephone: 908-740-4000
Emergency telephone number: 86-571-87268110
E-mail address: EHSDATASTEWARD@msd.com

Recommended use of the chemical and restrictions on use
Recommended use: Pharmaceutical

2. HAZARDS IDENTIFICATION

Emergency Overview
Appearance: granular
Colour: No data available
Odour: No data available

May cause damage to organs through prolonged or repeated exposure. Harmful to aquatic life with long lasting effects.

GHS Classification
Specific target organ toxicity - repeated exposure: Category 2
Long-term (chronic) aquatic hazard: Category 3

GHS label elements
Hazard pictograms:

Signal word: Warning

Hazard statements:
H373 May cause damage to organs through prolonged or repeated exposure.
H412 Harmful to aquatic life with long lasting effects.

Precautionary statements:
Prevention:
P260 Do not breathe dust.
Atorvastatin Formulation

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></td>
<td>Cellulose</td>
</tr>
<tr>
<td></td>
<td>Atorvastatin</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 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. 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.

5. FIREFIGHTING MEASURES

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

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)
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 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 spills 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.
7. HANDLING AND STORAGE

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 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.

Avoidance of contact: Oxidizing agents

Storage
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

Packaging material: Unsuitable material: None known.

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>PC-TWA</td>
<td>10 mg/m³</td>
<td>CN 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.

Eye/face 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.

Hand protection

Material
: Chemical-resistant gloves

Remarks
: Consider double gloving.

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
: granular

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
### 10. STABILITY AND REACTIVITY

<table>
<thead>
<tr>
<th>Property</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Reactivity</td>
<td>Not classified as a reactivity hazard.</td>
</tr>
<tr>
<td>Chemical stability</td>
<td>Stable under normal conditions.</td>
</tr>
<tr>
<td>Possibility of hazardous reactions</td>
<td>May form explosive dust-air mixture during processing, handling or other means. Can react with strong oxidizing agents.</td>
</tr>
<tr>
<td>Conditions to avoid</td>
<td>Heat, flames and sparks. Avoid dust formation.</td>
</tr>
<tr>
<td>Incompatible materials</td>
<td>Oxidizing agents</td>
</tr>
</tbody>
</table>

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**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

**Vapour pressure**: No data available

**Relative vapour 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.

**Molecular weight**: No data available

**Particle size**: No data available
Hazardous decomposition products: No hazardous decomposition products are known.

11. TOXICOLOGICAL INFORMATION

Exposure routes:
- 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:
- 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 sensitisation

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

Components:

Atorvastatin:
Test Type: Maximisation Test
Exposure routes: 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 foetal 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
SAFETY DATA SHEET
according to GB/T 16483 and GB/T 17519

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Effects on foetal development:
Species: Rat, female
Developmental Toxicity: NOAEL: 20 mg/kg body weight
Result: No teratogenic effects, Embryo-foetal toxicity
Remarks: Maternal toxicity observed.
Species: Rabbit, female
Application Route: Oral
Developmental Toxicity: NOAEL: 100 mg/kg body weight
Result: No embryo-foetal toxicity

STOT - single exposure
Not classified based on available information.

STOT - repeated exposure
May cause damage to organs through prolonged or repeated exposure.

Components:

Atorvastatin:
Exposure routes: 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

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

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

**Atorvastatin:**

Toxicity to fish

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

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

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

National Regulations

GB 6944/12268
Not regulated as a dangerous good

Special precautions for user
Not applicable

15. REGULATORY INFORMATION

National regulatory information
Law on the Prevention and Control of Occupational Diseases

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)
CN OEL : Occupational exposure limits for hazardous agents in the workplace - Chemical hazardous agents.
ACGIH / TWA : 8-hour, time-weighted average
CN OEL / PC-TWA : Permissible concentration - time weighted average

AICL - 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 Chemi-
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Disclaimer

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.

CN / EN