SAFETY DATA SHEET

Atorvastatin Formulation

1. PRODUCT AND COMPANY IDENTIFICATION

Product name: Atorvastatin Formulation

Manufacturer or supplier’s details
Company: MSD
Address: Briahnager - Off Pune Nagar Road
           Wagholi - Pune - India 412 207
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

Manufacture, Storage and Import of Hazardous Chemicals Rules 1989

Classification
Not classified as hazardous according to criteria laid down in Part I of Schedule-1.

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: Warning

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.

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>

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.

5. FIREFIGHTING MEASURES

Suitable extinguishing media: Water spray
Alcohol-resistant foam
Carbon dioxide (CO2)
Dry chemical
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Version 3.2  Revision Date: 09/13/2019  SDS Number: 187339-00009  Date of last issue: 24.04.2019

Date of first issue: 17.06.2015

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 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.

Local/Total ventilation: Use only with adequate ventilation.
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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 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>Atorvastatin</td>
<td>134523-03-8</td>
<td>TWA</td>
<td>0.05 mg/m³ (OEB 3)</td>
<td>Internal</td>
</tr>
</tbody>
</table>

Wipe limit: 0.5 mg/100 cm² Internal

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:
Material: Chemical-resistant gloves
Remarks: Consider double gloving.
Eye protection:
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...
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

<table>
<thead>
<tr>
<th>Property</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Appearance</td>
<td>granular</td>
</tr>
<tr>
<td>Colour</td>
<td>No data available</td>
</tr>
<tr>
<td>Odour</td>
<td>No data available</td>
</tr>
<tr>
<td>Odour Threshold</td>
<td>No data available</td>
</tr>
<tr>
<td>pH</td>
<td>No data available</td>
</tr>
<tr>
<td>Melting point/freezing point</td>
<td>No data available</td>
</tr>
<tr>
<td>Initial boiling point and boiling range</td>
<td>No data available</td>
</tr>
<tr>
<td>Flash point</td>
<td>No data available</td>
</tr>
<tr>
<td>Evaporation rate</td>
<td>No data available</td>
</tr>
<tr>
<td>Flammability (solid, gas)</td>
<td>May form explosive dust-air mixture during processing, handling or other means.</td>
</tr>
<tr>
<td>Flammability (liquids)</td>
<td>No data available</td>
</tr>
<tr>
<td>Upper explosion limit / Upper flammability limit</td>
<td>No data available</td>
</tr>
<tr>
<td>Lower explosion limit / Lower flammability limit</td>
<td>No data available</td>
</tr>
<tr>
<td>Vapour pressure</td>
<td>No data available</td>
</tr>
<tr>
<td>Relative vapour density</td>
<td>No data available</td>
</tr>
<tr>
<td>Density</td>
<td>No data available</td>
</tr>
</tbody>
</table>
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.

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
Method: Draize Test
Result: No eye irritation

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
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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

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 (Liver, muscle) through prolonged or repeated exposure if swallowed.

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

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 microorganisms:
EC50: > 1,000 mg/l
Exposure time: 3 h
Test Type: Respiration inhibition

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

Toxicity to daphnia and other aquatic invertebrates (Chronic toxicity):
NOEC: 0.2 mg/l
Exposure time: 21 d
Species: Daphnia magna (Water flea)
Method: OECD Test Guideline 211

Persistence and degradability

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

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

Mobility in soil

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

Transport in bulk according to IMO instruments
Not applicable for product as supplied.

15. REGULATORY INFORMATION

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

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)
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.

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