SAFETY DATA SHEET

Atorvastatin Formulation

SECTION 1: Identification of the substance/mixture and of the company/undertaking

1.1 Product identifier
Trade name: Atorvastatin Formulation

1.2 Relevant identified uses of the substance or mixture and uses advised against
Use of the Substance/Mixture: Pharmaceutical

1.3 Details of the supplier of the safety data sheet
Company: MSD
117 16th Road
1685 Halfway house, Midrand, South Africa
Telephone: +27 11 655 3000
E-mail address of person responsible for the SDS: EHSDATASTEWARD@msd.com

1.4 Emergency telephone number
+1-908-423-6000

SECTION 2: Hazards identification

2.1 Classification of the substance or mixture
Classification (REGULATION (EC) No 1272/2008)
Specific target organ toxicity - repeated exposure, Category 2
Long-term (chronic) aquatic hazard, Category 3
H373: May cause damage to organs through prolonged or repeated exposure.
H412: Harmful to aquatic life with long lasting effects.

2.2 Label elements
Labelling (REGULATION (EC) No 1272/2008)
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.
P273 Avoid release to the environment.
Response:
P314  Get medical advice/ attention if you feel unwell.

Hazardous components which must be listed on the label:
Atorvastatin

2.3 Other hazards
This substance/mixture contains no components considered to be either persistent, bioaccumulative and toxic (PBT), or very persistent and very bioaccumulative (vPvB) at levels of 0.1% or higher.
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

3.2 Mixtures

<table>
<thead>
<tr>
<th>Components</th>
<th>CAS-No.</th>
<th>EC-No. Index-No. Registration number</th>
<th>Classification</th>
<th>Concentration (% w/w)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Atorvastatin</td>
<td>134523-03-8</td>
<td></td>
<td>STOT RE 2; H373 (Liver, muscle) Aquatic Chronic 2; H411</td>
<td>&gt;= 10 - &lt; 20</td>
</tr>
</tbody>
</table>

For explanation of abbreviations see section 16.

SECTION 4: First aid measures

4.1 Description of 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.

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).

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.

4.2 Most important symptoms and effects, both acute and delayed
Risks: 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.

4.3 Indication of any immediate medical attention and special treatment needed
Treatment: Treat symptomatically and supportively.

SECTION 5: Firefighting measures

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

Unsuitable extinguishing media: None known.

5.2 Special hazards arising from the substance or mixture
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

5.3 Advice for firefighters
Special protective equipment for firefighters: In the event of fire, wear self-contained breathing apparatus. Use personal protective equipment.
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.
SECTION 6: Accidental release measures

6.1 Personal precautions, protective equipment and emergency procedures

Personal precautions: Use personal protective equipment. Follow safe handling advice (see section 7) and personal protective equipment recommendations (see section 8).

6.2 Environmental precautions

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.

6.3 Methods and material for containment and cleaning up

Methods for 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.

6.4 Reference to other sections

See sections: 7, 8, 11, 12 and 13.

SECTION 7: Handling and storage

7.1 Precautions for safe 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.

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.

7.2 Conditions for safe storage, including any incompatibilities

Requirements for storage areas and containers: Keep in properly labelled containers. Store in accordance with the particular national regulations.

Advice on common storage: Do not store with the following product types: Strong oxidizing agents

7.3 Specific end use(s)

Specific use(s): No data available

SECTION 8: Exposure controls/personal protection

8.1 Control parameters

<table>
<thead>
<tr>
<th>Components</th>
<th>CAS-No.</th>
<th>Value type (Form of exposure)</th>
<th>Control parameters</th>
<th>Basis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cellulose</td>
<td>9004-34-6</td>
<td>TWA OEL-RL (Respirable dust)</td>
<td>5 mg/m³</td>
<td>ZA OEL</td>
</tr>
<tr>
<td></td>
<td></td>
<td>TWA OEL-RL (Inhalable dust)</td>
<td>10 mg/m³</td>
<td>ZA OEL</td>
</tr>
<tr>
<td></td>
<td></td>
<td>STEL OEL-RL (Dust)</td>
<td>20 mg/m³</td>
<td>ZA OEL</td>
</tr>
</tbody>
</table>

Further information: Recommended Limit

Atorvastatin | 134523-03-8 | TWA | 0.05 mg/m³ (OEB 3) | Internal |
|             |           | Wipe limit | 0.5 mg/100 cm² | Internal |

Derived No Effect Level (DNEL) according to Regulation (EC) No. 1907/2006:

<table>
<thead>
<tr>
<th>Substance name</th>
<th>End Use</th>
<th>Exposure routes</th>
<th>Potential health effects</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Calcium carbonate</td>
<td>Workers</td>
<td>Inhalation</td>
<td>Long-term systemic effects</td>
<td>6.36 mg/m³</td>
</tr>
<tr>
<td></td>
<td>Consumers</td>
<td>Ingestion</td>
<td>Acute systemic effects</td>
<td>6.1 mg/kg bw/day</td>
</tr>
<tr>
<td></td>
<td>Consumers</td>
<td>Inhalation</td>
<td>Long-term systemic effects</td>
<td>1.06 mg/m³</td>
</tr>
</tbody>
</table>
Consumers

Ingestion

Long-term systemic effects

Predicted No Effect Concentration (PNEC) according to Regulation (EC) No. 1907/2006:

<table>
<thead>
<tr>
<th>Substance name</th>
<th>Environmental Compartment</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Calcium carbonate</td>
<td>Sewage treatment plant</td>
<td>100 mg/l</td>
</tr>
</tbody>
</table>

8.2 Exposure controls

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

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.

Hand protection

Material: Chemical-resistant gloves

Remarks: Consider double gloving.

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.

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 (P)

SECTION 9: Physical and chemical properties

9.1 Information on basic 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

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.

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.

9.2 Other information

Flammability (liquids) : No data available

Molecular weight : No data available

Particle size : No data available

SECTION 10: Stability and reactivity

10.1 Reactivity
Not classified as a reactivity hazard.

10.2 Chemical stability
Stable under normal conditions.

10.3 Possibility of hazardous reactions
Hazardous reactions : May form explosive dust-air mixture during processing, handling or other means. Can react with strong oxidizing agents.

10.4 Conditions to avoid
Conditions to avoid: Heat, flames and sparks. Avoid dust formation.

10.5 Incompatible materials
Materials to avoid: Oxidizing agents

10.6 Hazardous decomposition products
No hazardous decomposition products are known.

SECTION 11: Toxicological information

11.1 Information on toxicological effects
Information on likely routes of exposure:
- Inhalation
- Skin contact
- Ingestion
- Eye contact

Acute toxicity
Not classified based on available information.

Components:
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:**

**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:**

**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:**

**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 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:**

**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

12.1 Toxicity

Components:

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)
12.2 Persistence and degradability

**Components:**

**Atorvastatin:**

12.3 Bioaccumulative potential

**Components:**

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

12.4 Mobility in soil

**Components:**

**Atorvastatin:**
- Distribution among environmental compartments: log Koc: 2.84

12.5 Results of PBT and vPvB assessment

**Product:**
- Assessment: This substance/mixture contains no components considered to be either persistent, bioaccumulative and toxic (PBT), or very persistent and very bioaccumulative (vPvB) at levels of 0.1% or higher.

12.6 Other adverse effects

**Product:**
- Endocrine disrupting potential: The substance/mixture does not contain components considered to have endocrine disrupting properties according to REACH Article 57(f) or Commission Delegated regulation (EU) 2017/2100 or Commission Regulation (EU) 2018/605 at levels of 0.1% or higher.

SECTION 13: Disposal considerations

13.1 Waste treatment methods

**Product:**
- Dispose of in accordance with local regulations. According to the European Waste Catalogue, Waste Codes are not product specific, but application specific. Waste codes should be assigned by the user, preferably in discussion with the waste disposal authorities.
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

14.1 UN number
Not regulated as a dangerous good

14.2 UN proper shipping name
Not regulated as a dangerous good

14.3 Transport hazard class(es)
Not regulated as a dangerous good

14.4 Packing group
Not regulated as a dangerous good

14.5 Environmental hazards
Not regulated as a dangerous good

14.6 Special precautions for user
Not applicable

14.7 Transport in bulk according to Annex II of Marpol and the IBC Code
 Remarks: Not applicable for product as supplied.

SECTION 15: Regulatory information

15.1 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

15.2 Chemical safety assessment
A Chemical Safety Assessment has not been carried out.

SECTION 16: Other information

Other information: Items where changes have been made to the previous version are highlighted in the body of this document by two vertical lines.

Full text of H-Statements

- H373: May cause damage to organs through prolonged or repeated exposure if swallowed.
- H411: Toxic to aquatic life with long lasting effects.

Full text of other abbreviations
SAFETY DATA SHEET

Atorvastatin Formulation

Version: 2.5
Revision Date: 09.04.2021
SDS Number: 184709-00012
Date of last issue: 10.10.2020
Date of first issue: 17.06.2015

Aquatic Chronic: Long-term (chronic) aquatic hazard
STOT RE: Specific target organ toxicity - repeated exposure
ZA OEL: South Africa. Hazardous Chemical Substances Regulations, Occupational Exposure Limits
ZA OEL / TWA OEL-RL: Long term occupational exposure limits - recommended limit
ZA OEL / STEL OEL-RL: Short term occupational exposure limits - recommended limit

ADN - European Agreement concerning the International Carriage of Dangerous Goods by Inland Waterways; ADR - European Agreement concerning the International Carriage of Dangerous Goods by Road; AIIRC - Australian Inventory of Industrial Chemicals; ASTM - American Society for the Testing of Materials; bw - Body weight; CLP - Classification Labelling Packaging Regulation; Regulation (EC) No 1272/2008; CMR - Carcinogen, Mutagen or Reproductive Toxicant; DIN - Standard of the German Institute for Standardisation; DSL - Domestic Substances List (Canada); ECHA - European Chemicals Agency; EC-Number - European Community number; 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; GHS - Globally Harmonized System; 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; IC50 - Half maximal inhibitory concentration; ICAO - International Civil Aviation Organization; IECSC - Inventory of Existing Chemical Substances in China; IMPD - International Maritime Dangerous Goods; NOEC - No Observed (Adverse) Effect Concentration; NO(A)EC - No Observed (Adverse) Effect Concentration; NO(A)EL - No Observed (Adverse) Effect Level; NOELR - No Observable Effect Loading Rate; 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; RID - Regulations concerning the International Carriage of Dangerous Goods by Rail; SADT - Self-Accelerating Decomposition Temperature; SDS - Safety Data Sheet; SVHC - Substance of very high concern; TCSI - Taiwan Chemical Substance Inventory; 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

Further information

Classification of the mixture:

| STOT RE 2 | H373 | Calculation method |
| Aquatic Chronic 3 | H412 | Calculation method |

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.

ZA / EN