SAFETY DATA SHEET

Atorvastatin Formulation

Section 1: Identification

Product name : Atorvastatin Formulation

Manufacturer or supplier's details

Company : MSD
Address : 33 Whakatiki Street - Private Bag 908 Upper Hutt - New Zealand
Telephone : +1-908-740-4000
Emergency telephone number : +1-908-423-6000
E-mail address : EHSDATASTEWARD@msd.com

Recommended use of the chemical and restrictions on use

Recommended use : Pharmaceutical

Section 2: Hazard identification

GHS Classification

Specific target organ toxicity - repeated exposure (Oral) : Category 2 (Liver, muscle)

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.

Precautionary statements : Prevention:
P260 Do not breathe dust.

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>
<th>CAS-No.</th>
<th>Concentration (% w/w)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Calcium carbonate</td>
<td>Calcium carbonate</td>
<td>471-34-1</td>
<td>&gt;= 30 - &lt; 60</td>
</tr>
<tr>
<td>Cellulose</td>
<td>Cellulose</td>
<td>9004-34-6</td>
<td>&gt;= 10  - &lt; 30</td>
</tr>
<tr>
<td>Atorvastatin</td>
<td>Atorvastatin</td>
<td>134523-03-8</td>
<td>&gt;= 10 - &lt; 30</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 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.

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
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 labelled 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

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>Calcium carbonate</td>
<td>471-34-1</td>
<td>WES-TWA</td>
<td>10 mg/m³ (Calcium carbonate)</td>
<td>NZ OEL</td>
</tr>
<tr>
<td>Cellulose</td>
<td>9004-34-6</td>
<td>WES-TWA</td>
<td>10 mg/m³</td>
<td>NZ 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

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.
Skin and body protection: Wear a faceshield or other full face protection if there is a potential for direct contact to the face with dusts, mists, or aerosols.

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
- **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.
- **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)**: No data available
  - **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

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
Exposure routes : Inhalation
  Skin contact
  Ingestion
  Eye contact

Acute toxicity
  Not classified based on available information.
Components:
Calcium carbonate:
  Acute oral toxicity : LD50 (Rat): > 2,000 mg/kg
    Method: OECD Test Guideline 420
    Assessment: The substance or mixture has no acute oral toxicity
Acute inhalation toxicity : LC50 (Rat): > 3 mg/l
    Exposure time: 4 h
    Test atmosphere: dust/mist
    Method: OECD Test Guideline 403
    Assessment: The substance or mixture has no acute inhalation toxicity
Acute dermal toxicity : LD50 (Rat): > 2,000 mg/kg
    Method: OECD Test Guideline 402
Assessment: The substance or mixture has no acute dermal toxicity

**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:**

**Calcium carbonate:**
Species : Rabbit
Method : OECD Test Guideline 404
Result : No skin irritation

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

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

**Components:**

**Calcium carbonate:**
Species : Rabbit
Result : No eye irritation
Method : OECD Test Guideline 405

**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:**

**Calcium carbonate:**
- **Test Type:** Local lymph node assay (LLNA)
- **Exposure routes:** Skin contact
- **Species:** Mouse
- **Method:** OECD Test Guideline 429
- **Result:** negative

**Atorvastatin:**
- **Test Type:** Maximisation Test
- **Exposure routes:** Skin contact
- **Species:** Guinea pig
- **Result:** negative

**Chronic toxicity**

**Germ cell mutagenicity**
Not classified based on available information.

**Components:**

**Calcium carbonate:**
- **Genotoxicity in vitro**
  - **Test Type:** Bacterial reverse mutation assay (AMES)
  - **Method:** OECD Test Guideline 471
  - **Result:** negative

  **Test Type:** Chromosome aberration test in vitro
  **Method:** OECD Test Guideline 473
  **Result:** negative

  **Test Type:** In vitro mammalian cell gene mutation test
  **Method:** OECD Test Guideline 476
  **Result:** negative

**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:

Calcium carbonate:
Effects on fertility: Test Type: Combined repeated dose toxicity study with the
reproduction/developmental toxicity screening test
Species: Rat
Application Route: Ingestion
Method: OECD Test Guideline 422
Result: negative

Effects on foetal development
Species: Rat
Application Route: Ingestion
Method: OECD Test Guideline 414
Result: negative

Cellulose:
Effects on fertility
Species: Rat
Application Route: Ingestion
Result: negative

Effects on foetal development
Species: Rat
Application Route: Ingestion
Result: negative

Atorvastatin:
Effects on fertility
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 fertility
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:**

**Calcium carbonate:**
- Species: Rat
- NOAEL: ≥ 1,000 mg/kg
- Application Route: Ingestion
- Exposure time: 28 Days
- Method: OECD Test Guideline 422

**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:

Calcium carbonate:

Toxicity to fish:
- LL50 (Oncorhynchus mykiss (rainbow trout)): > 100 mg/l
  Exposure time: 96 h
  Test substance: Water Accommodated Fraction
  Method: OECD Test Guideline 203

Toxicity to daphnia and other aquatic invertebrates:
- EL50 (Daphnia magna (Water flea)): > 100 mg/l
  Exposure time: 48 h
  Test substance: Water Accommodated Fraction
  Method: OECD Test Guideline 202

Toxicity to algae/aquatic plants:
- NOELR (Pseudokirchneriella subcapitata (green algae)): 50 mg/l
  Exposure time: 72 h
  Test substance: Water Accommodated Fraction
  Method: OECD Test Guideline 201
- EL50 (Pseudokirchneriella subcapitata (green algae)): > 100 mg/l
  Exposure time: 72 h
  Test substance: Water Accommodated Fraction
  Method: OECD Test Guideline 201

Toxicity to microorganisms:
- NOEC: 1,000 mg/l
  Exposure time: 3 h
  Method: OECD Test Guideline 209

  EC50: > 1,000 mg/l
  Exposure time: 3 h
  Method: OECD Test Guideline 209

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.

National Regulations
- NZS 5433
  Not regulated as a dangerous good

Section 15: Regulatory information

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

HSNO Approval Number
- HSR100425 Pharmaceutical Active Ingredients Group Standard 2017

HSW Controls
- Certified handler certificate not required.
- Tracking hazardous substance not required.
- Refer to the Health and Safety at Work (Hazardous Substances) Regulations 2017, for further information.

The components of this product are reported in the following inventories:
- AICS: not determined
- DSL: not determined
- IECSC: not determined
Section 16: Other information

Further information

Date format: dd.mm.yyyy

Full text of other abbreviations
ACGIH: USA. ACGIH Threshold Limit Values (TLV)
NZ OEL: New Zealand. Workplace Exposure Standards for Atmospheric Contaminants

ACGIH / TWA: 8-hour, time-weighted average
NZ OEL / WES-TWA: Workplace Exposure Standard - Time Weighted average

AIIC - 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 Civil Aviation Organization; 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 Chemicals and 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; 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.

NZ / EN