1. PRODUCT AND COMPANY IDENTIFICATION

Product name : Alendronate Solid 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
Acute toxicity (Oral) : Category 5
Skin corrosion/irritation : Category 2
Serious eye damage/eye irritation : Category 1
Reproductive toxicity : Category 2
Specific target organ toxicity - single exposure : Category 3
Specific target organ toxicity - repeated exposure : Category 2 (Bone, Stomach, Kidney)
Short-term (acute) aquatic hazard : Category 3

GHS label elements
Hazard pictograms:

Signal word: Danger

Hazard statements:
- H303 May be harmful if swallowed.
- H315 Causes skin irritation.
- H318 Causes serious eye damage.
- H335 May cause respiratory irritation.
- H361d Suspected of damaging the unborn child.
- H373 May cause damage to organs (Bone, Stomach, Kidney) through prolonged or repeated exposure.
- H402 Harmful to aquatic life.

Precautionary statements:

Prevention:
- P203 Obtain, read and follow all safety instructions before use.
- P260 Do not breathe dust.
- P264 Wash skin thoroughly after handling.
- P271 Use only outdoors or in a well-ventilated area.
- P273 Avoid release to the environment.
- P280 Wear protective gloves/ protective clothing/ eye protection/ face protection.

Response:
- P301 + P332 + P317 IF SWALLOWED or if skin irritation occurs: Get medical help.
- P302 + P352 IF ON SKIN: Wash with plenty of water.
- P304 + P340 + P319 IF INHALED: Remove person to fresh air and keep comfortable for breathing. Get medical help if you feel unwell.
- P305 + P354 + P338 + P317 IF IN EYES: Immediately rinse with water for several minutes. Remove contact lenses, if present and easy to do. Continue rinsing. Get medical help.
- P318 IF exposed or concerned, get medical advice.
- P362 + P364 Take off contaminated clothing and wash it before reuse.

Storage:
- P405 Store locked up.

Disposal:
- P501 Dispose of contents/ container to an approved waste disposal plant.

Other hazards which do not result in classification
May form explosive dust-air mixture during processing, handling or other means.

3. COMPOSITION/INFORMATION ON INGREDIENTS

Substance / Mixture: Mixture

Components
SAFETY DATA SHEET
Alendronate Solid Formulation

Version 4.4  Revision Date: 16.10.2020  SDS Number: 22294-00016  Date of last issue: 23.03.2020  Date of first issue: 15.10.2014

<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;= 30 - &lt; 50</td>
</tr>
<tr>
<td>Alendronate</td>
<td>121268-17-5</td>
<td>&gt;= 25 - &lt; 30</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.

In case of skin contact: In case of contact, immediately flush skin with plenty of water for at least 15 minutes while removing contaminated clothing and shoes. Get medical attention. Wash clothing before reuse. Thoroughly clean shoes before reuse.

In case of eye contact: In case of contact, immediately flush eyes with plenty of water for at least 15 minutes. If easy to do, remove contact lens, if worn. Get medical attention immediately.

If swallowed: If swallowed, DO NOT induce vomiting. Get medical attention. Rinse mouth thoroughly with water.

Most important symptoms and effects, both acute and delayed: May be harmful if swallowed. Causes skin irritation. Causes serious eye damage. May cause respiratory irritation. Suspected of damaging the unborn child. May cause damage to organs through prolonged or repeated exposure.

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)  Phosphorus 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 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: If sufficient ventilation is unavailable, use with local exhaust ventilation.

Advice on safe handling: Do not get on skin or clothing. Do not breathe dust. Do not swallow. Do not get in eyes. Wash skin thoroughly after handling. Handle in accordance with good industrial hygiene and safety practice, based on the results of the workplace exposure assessment. Keep container tightly closed.
Already sensitised individuals should consult their physician regarding working with respiratory irritants or sensitisers.

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 locked up.

Keep tightly closed.

Keep in a cool, well-ventilated place.

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>Alendronate</td>
<td>121268-17-5</td>
<td>TWA</td>
<td>20 µg/m³ (OEB 3)</td>
<td>Internal</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Wipe limit</td>
<td>200 µg/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
- **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.

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 : powder
Colour : white
Odour : odourless
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 : Not applicable
Evaporation rate : Not applicable
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 : Not applicable
Relative density : No data available
Density : 1 g/cm³
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

11. TOXICOLOGICAL INFORMATION

Information on likely routes of exposure: Inhalation, Skin contact, Ingestion, Eye contact

Acute toxicity: May be harmful if swallowed.

Product:
Acute oral toxicity: Acute toxicity estimate: 2,115 mg/kg
Method: Calculation method

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

**Alendronate:**
Acute oral toxicity : LD50 (Rat): 552 - 626 mg/kg
LD50 (Mouse): 966 - 1,280 mg/kg

Acute inhalation toxicity : Remarks: No data available
Acute dermal toxicity : Remarks: No data available

**Skin corrosion/irritation**
Causes skin irritation.

**Components:**

**Alendronate:**
Species : Rabbit
Remarks : Severe skin irritation

**Serious eye damage/eye irritation**
Causes serious eye damage.

**Components:**

**Alendronate:**
Species : Rabbit
Result : Severe irritation

**Respiratory or skin sensitisation**

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

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

**Components:**

**Alendronate:**
Remarks : No data available

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

**Components:**

**Cellulose:**
Genotoxicity in vitro : Test Type: Bacterial reverse mutation assay (AMES)
Result: negative
Alendronate Solid Formulation

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

Alendronate:
Genotoxicity in vitro: Test Type: Alkaline elution assay  
Test system: rat hepatocytes  
Result: negative

Test Type: Bacterial reverse mutation assay (AMES)  
Metabolic activation: with and without metabolic activation  
Result: negative

Test Type: In vitro mammalian cell gene mutation test  
Result: negative

Test Type: Chromosomal aberration  
Test system: Chinese hamster ovary cells  
Result: equivocal

Genotoxicity in vivo: Test Type: Chromosomal aberration  
Species: Mouse  
Result: negative

Carcinogenicity
Not classified based on available information.

Components:

Cellulose:
Species: Rat  
Application Route: Ingestion  
Exposure time: 72 weeks  
Result: negative

Alendronate:
Species: Rat, male  
Application Route: Oral  
Exposure time: 2 Years  
1 mg/kg body weight  
3.75 mg/kg body weight  
Target Organs: Thyroid  
Remarks: The mechanism or mode of action may not be relevant in humans.
Reproductive toxicity
Suspected of damaging the unborn child.

**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

**Alendronate:**
Effects on fertility
- Test Type: Fertility
- Species: Rat, male and female
- Application Route: Oral
- Fertility: NOAEL: 5 mg/kg body weight
- Result: Animal testing did not show any effects on fertility.

Effects on foetal development
- Test Type: Development
- Species: Rat, female
- Application Route: Oral
- Developmental Toxicity: LOAEL: 1 - 15 mg/kg body weight
- Symptoms: Reduced number of viable fetuses, Reduced body weight, Skeletal malformations
- Result: Embryotoxic effects and adverse effects on the offspring were detected.
- Test Type: Development
- Species: Rabbit, female
- Application Route: Oral
- Developmental Toxicity: NOAEL: 40 mg/kg body weight
- Result: No adverse effects

Reproductive toxicity - Assessment
- Some evidence of adverse effects on development, based on animal experiments.

**STOT - single exposure**
May cause respiratory irritation.

**Components:**

**Alendronate:**
Assessment
- May cause respiratory irritation.

**STOT - repeated exposure**
May cause damage to organs (Bone, Stomach, Kidney) through prolonged or repeated exposure.
SAFETY DATA SHEET

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Components:

Alendronate:
Target Organs: Bone, Stomach, Kidney
Assessment: May cause damage to organs through prolonged or repeated exposure.

Repeated dose toxicity

Components:

Cellulose:
Species: Rat
NOAEL: \( \geq 9,000 \text{ mg/kg} \)
Application Route: Ingestion
Exposure time: 90 Days

Alendronate:
Species: Rat
NOAEL: 2.5 mg/kg
LOAEL: > 2.5 mg/kg
Application Route: Intravenous
Exposure time: 53 Weeks
Target Organs: Stomach

Species: Dog
LOAEL: 0.01 mg/kg
Application Route: Intravenous
Exposure time: 3 yr
Target Organs: Stomach, Bone, Kidney

Species: Dog
NOAEL: 2 mg/kg
LOAEL: 4 mg/kg
Application Route: Oral
Exposure time: 53 Weeks
Target Organs: Kidney

Aspiration toxicity
Not classified based on available information.

Components:

Alendronate:
Not applicable

Experience with human exposure

Components:

Alendronate:
Inhalation: Symptoms: respiratory tract irritation
Skin contact: Symptoms: Severe irritation, skin blistering
SAFETY DATA SHEET

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Eye contact: Symptoms: Severe irritation
Ingestion: Symptoms: Gastrointestinal disturbance, musculoskeletal pain

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

Alendronate:
Toxicity to fish: LC₅₀ (Pimephales promelas (fathead minnow)): 27 mg/l
Exposure time: 96 h
Method: OECD Test Guideline 203

LC₅₀ (Oncorhynchus mykiss (rainbow trout)): > 1,000 mg/l
Exposure time: 96 h
Method: FDA 4.11

Toxicity to daphnia and other aquatic invertebrates: EC₅₀ (Daphnia magna (Water flea)): 170 mg/l
Exposure time: 48 h
Method: OECD Test Guideline 202

Toxicity to algae/aquatic plants: ErC₅₀ (Pseudokirchneriella subcapitata (green algae)): > 10 mg/l
Exposure time: 72 h
Method: OECD Test Guideline 201

NOEC (Pseudokirchneriella subcapitata (green algae)): 4 mg/l
Exposure time: 72 h
Method: OECD Test Guideline 201

Toxicity to fish (Chronic toxicity): NOEC: 1.1 mg/l
Exposure time: 32 d
Species: Pimephales promelas (fathead minnow)
Method: OECD Test Guideline 210

LOEC: 1.9 mg/l
Exposure time: 32 d
Species: Pimephales promelas (fathead minnow)
Method: OECD Test Guideline 210

Toxicity to daphnia and other aquatic invertebrates (Chronic toxicity): NOEC: 4.7 mg/l
Exposure time: 21 d
Species: Daphnia magna (Water flea)
Method: OECD Test Guideline 211
Persistence and degradability

Components:

Cellulose:
Biodegradability: Result: Readily biodegradable.

Alendronate:
Biodegradability: Result: Readily biodegradable.

Biodegradation: 70.3 %
Exposure time: 7 d

Stability in water: Degradation half life (DT50): 375 d
Method: OECD Test Guideline 111

Bioaccumulative potential

Components:

Alendronate:
Partition coefficient: n-octanol/water: log Pow: -1.73

Mobility in soil
No data available

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.
SAFETY DATA SHEET

Alendronate Solid Formulation

Version 4.4  
Revision Date: 16.10.2020  
SDS Number: 22294-00016  
Date of last issue: 23.03.2020  
Date of first issue: 15.10.2014

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

Sources of key data used to compile the Safety Data Sheet:


Date format: dd.mm.yyyy

Full text of other abbreviations

ACGIH: USA. ACGIH Threshold Limit Values (TLV)

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

AIIIC - 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 - Trans-
portation 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.

IN / EN