SECTION 1. PRODUCT AND COMPANY IDENTIFICATION

Product name: Alendronate Solid Formulation

Manufacturer or supplier's details
Company: Organon & Co.
Address: Rua Treze de Maio, 1161
Campinas, São Paulo, Brazil B-2220
Telephone: 551-430-6000
Emergency telephone: 215-631-6999
E-mail address: EHSSTEWARD@organon.com

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

SECTION 2. HAZARDS IDENTIFICATION

GHS Classification in accordance with ABNT NBR 14725 Standard
Acute toxicity (Oral): Category 5
Skin irritation: Category 2
Serious eye damage: 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 in accordance with ABNT NBR 14725 Standard
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:
P201 Obtain special instructions before use.
P260 Do not breathe dust.
P264 Wash skin thoroughly after handling.
P273 Avoid release to the environment.
P280 Wear protective gloves/ protective clothing/ eye protection/ face protection.

Response:
P305 + P351 + P338 + P310 IF IN EYES: Rinse cautiously with water for several minutes. Remove contact lenses, if present and easy to do. Continue rinsing. Immediately call a POISON CENTER/ doctor.

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

SECTION 3. COMPOSITION/INFORMATION ON INGREDIENTS

Substance / Mixture : Mixture

Components

<table>
<thead>
<tr>
<th>Chemical name</th>
<th>CAS-No.</th>
<th>Classification</th>
<th>Concentration (% w/w)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cellulose</td>
<td>9004-34-6</td>
<td></td>
<td>&gt;= 30 -&lt; 50</td>
</tr>
</tbody>
</table>
| Alendronate   | 121268-17-5 | Acute toxicity (Oral), Category 4
Skin irritation, Category 2
Serious eye damage, Category 1
Reproductive toxicity, Category 2
Specific target organ toxicity - single exposure, Category 3
Specific target organ toxicity - repeated exposure (Bone, Stomach, Kidney), Category 2
Short-term (acute) aquatic hazard, Category 3 | >= 25 -< 30                          |

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.

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.

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)
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.
## 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
- 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 sensitized individuals should consult their physician regarding working with respiratory irritants or sensitizers.
- 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.

Conditions for safe storage: Keep in properly labeled 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

SECTION 8. EXPOSURE CONTROLS/PERSONAL PROTECTION

Ingredients 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></td>
<td>Wipe limit 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
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.
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.

SECTION 9. PHYSICAL AND CHEMICAL PROPERTIES

Appearance: powder
Color: white
Odor: odorless
Odor 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
Vapor pressure: No data available
Relative vapor density: Not applicable
Relative density: No data available
Density: 1 g/cm³
Solubility(ies)
   Water solubility: No data available
Partition coefficient: n-octanol/water: Not applicable
Autoignition temperature: No data available
Decomposition temperature : No data available
Viscosity
Viscosity, kinematic : Not applicable
Explosive properties : Not explosive
Oxidizing properties : The substance or mixture is not classified as oxidizing.
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

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 sensitization**

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

**Respiratory sensitization**
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

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 fetal 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 fetal 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.

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

**SECTION 12. ECOLOGICAL INFORMATION**

**Ecotoxicity**

**Components:**

**Cellulose:**  
Toxicity to fish: \( \text{LC50 (Oryzias latipes (Japanese medaka))}: > 100 \text{ mg/l} \)  
Exposure time: 48 h
Alendronate Solid Formulation

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 (Pimephales promelas (fathead minnow)): 1,1 mg/l
Exposure time: 32 d
Method: OECD Test Guideline 210

LOEC (Pimephales promelas (fathead minnow)): 1,9 mg/l
Exposure time: 32 d
Method: OECD Test Guideline 210

**Toxicity to daphnia and other aquatic invertebrates (Chronic toxicity)**

NOEC (Daphnia magna (Water flea)): 4,7 mg/l
Exposure time: 21 d
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

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.

Domestic regulation

ANTT
Not regulated as a dangerous good

SECTION 15. REGULATORY INFORMATION

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

National List of Carcinogenic Agents for Humans - (LINACH): Not applicable

Brazil. List of chemicals controlled by the Federal Police: Not applicable
SECTI ON 16. OTHER INFORMATION

Further information

Full text of other abbreviations
ACGIH: USA. ACGIH Threshold Limit Values (TLV)
ACGIH / TWA: 8-hour, time-weighted average

All abbreviations:
AICS - 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; ICDG - 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; PICTS - 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.

BR / Z8