SAFETY DATA SHEET

Alendronate Liquid Formulation

SECTION 1. PRODUCT AND COMPANY IDENTIFICATION

Product name : Alendronate Liquid Formulation

Manufacturer or supplier’s details
Company : MSD
Address : 855 Leandro N. Alem St., 8 Floor
Buenos Aires, Argentina C1001AFB
Telephone : 908-740-4000
Emergency telephone : 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

SECTION 2. HAZARDS IDENTIFICATION

GHS Classification
Not a hazardous substance or mixture.

GHS label elements
Not a hazardous substance or mixture.

Other hazards which do not result in classification
None known.

SECTION 3. COMPOSITION/INFORMATION ON INGREDIENTS

Substance / Mixture : Mixture

Components

<table>
<thead>
<tr>
<th>Chemical name</th>
<th>CAS-No.</th>
<th>Concentration (% w/w)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Alendronate</td>
<td>121268-17-5</td>
<td>&gt;= 0,1 -&lt; 0,25</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.

In case of skin contact : In case of contact, immediately flush skin with soap and plenty of water.
Remove contaminated clothing and shoes.
Get medical attention.
Wash clothing before reuse.
Thoroughly clean shoes before reuse.

In case of eye contact: Flush eyes with water as a precaution.
Get medical attention if irritation develops and persists.

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:
None known.

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 fire fighting:
Exposure to combustion products may be a hazard to health.

Hazardous combustion products:
Carbon oxides
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 fire-fighters:
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 and personal protective equipment recommendations.

Environmental precautions:
Discharge into the environment must be avoided.
Prevent further leakage or spillage if safe to do so.
Prevent spreading over a wide area (e.g., by containment or oil barriers).
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:
Soak up with inert absorbent material.
For large spills, provide diking or other appropriate
containment to keep material from spreading. If diked material can be pumped, store recovered material in appropriate container. Clean up remaining materials from spill with suitable absorbent. 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 : See Engineering measures under EXPOSURE CONTROLS/PERSONAL PROTECTION section.
Local/Total ventilation : Use only with adequate ventilation.
Advice on safe handling : Avoid inhalation of vapor or mist.
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
Take care to prevent spills, waste and minimize release to the environment.

Conditions for safe storage : Keep in properly labeled 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

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>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 : Use appropriate engineering controls and manufacturing technologies to control airborne concentrations (e.g., dripless quick connections).
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 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.

SECTION 9. PHYSICAL AND CHEMICAL PROPERTIES

Appearance: liquid
Color: clear
Odor: No data available
Odor Threshold: No data available
pH: 6.4 - 7.2
Melting point/freezing point: No data available
Initial boiling point and boiling range: 100 °C
Flash point: No data available
Evaporation rate: No data available
Flammability (solid, gas): Not applicable
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 : No data available
Relative density : No data available
Density : No data available
Solubility(ies)
  Water solubility : soluble
Partition coefficient: n-octanol/water : Not applicable
Autoignition 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.
Particle size : Not applicable

SECTION 10. STABILITY AND REACTIVITY

Reactivity : Not classified as a reactivity hazard.
Chemical stability : Stable under normal conditions.
Possibility of hazardous reactions : Can react with strong oxidizing agents.
Conditions to avoid : None known.
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
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Version 4.7 Revision Date: 13.09.2019 SDS Number: 28183-00015 Date of last issue: 24.04.2019 Date of first issue: 05.11.2014

Acute toxicity
Not classified based on available information.

Components:
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
Not classified based on available information.

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

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

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:
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:
Species: Mouse
Result: negative

Carcinogenicity
Not classified based on available information.

Components:

Alendronate:
Species: Rat, male
Application Route: Oral
Exposure time: 2 Years
Target Organs: Thyroid
Remarks: The mechanism or mode of action may not be relevant in humans.

Reproductive toxicity
Not classified based on available information.

Components:

Alendronate:
Effects on 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:
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.
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**
Not classified based on available information.

**Components:**

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

**STOT-repeated exposure**
Not classified based on available information.

**Components:**

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

**Repeated dose toxicity**

**Components:**

**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

### Product:

<table>
<thead>
<tr>
<th>Route</th>
<th>Symptoms</th>
</tr>
</thead>
<tbody>
<tr>
<td>Inhalation</td>
<td>Symptoms: respiratory tract irritation</td>
</tr>
<tr>
<td>Skin contact</td>
<td>Symptoms: May cause, Skin irritation</td>
</tr>
<tr>
<td>Eye contact</td>
<td>Symptoms: May cause, Eye irritation</td>
</tr>
<tr>
<td>Ingestion</td>
<td>Symptoms: Gastrointestinal disturbance, musculoskeletal pain</td>
</tr>
</tbody>
</table>

## Ecotoxicity

### Components:

#### 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                                                       |
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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:
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.
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SECTION 15. REGULATORY INFORMATION

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

Argentina. Carcinogenic Substances and Agents Registry: Not applicable

Control of precursors and essential chemicals for the preparation of drugs: Not applicable

International Regulations

The ingredients of this product are reported in the following inventories:

AICS: not determined
DSL: not determined
IECS: not determined

SECTION 16. OTHER INFORMATION

Further information


Full text of other abbreviations

AICS - Australian Inventory of Chemical Substances; 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 Develop-
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