SAFETY DATA SHEET

Alendronate / Vitamin D Formulation

SECTION 1. PRODUCT AND COMPANY IDENTIFICATION

Product name: Alendronate / Vitamin D Formulation

Manufacturer or supplier's details

Company name of supplier: MSD
Address: Avenida 16 de Septiembre No. 301
Xaltocan - Xochimilco Mexico 16090

Telephone: 52 55 57284444
Telefax: 908-735-1496
Emergency telephone: 1-908-423-6000
E-mail address: EHSDATASTEWARD@msd.com

Recommended use of the chemical and restrictions on use

Recommended use: Pharmaceutical

SECTION 2. HAZARDS IDENTIFICATION

GHS Classification

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: Category 2 (Bone, Stomach, Kidney)

GHS label elements

Hazard pictograms:

Signal Word: Danger
Hazard Statements:
H302 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.

Precautionary Statements:
Prevention:
P201 Obtain special instructions before use.
P202 Do not handle until all safety precautions have been read and understood.
P260 Do not breathe dust.
P264 Wash skin thoroughly after handling.
P270 Do not eat, drink or smoke when using this product.
P271 Use only outdoors or in a well-ventilated area.
P280 Wear protective gloves/ protective clothing/ eye protection/ face protection.

Response:
P301 + P312 + P330 IF SWALLOWED: Call a POISON CENTER or doctor/ physician if you feel unwell. Rinse mouth.
P302 + P352 IF ON SKIN: Wash with plenty of water.
P304 + P340 + P312 IF INHALED: Remove victim to fresh air and keep at rest in a position comfortable for breathing. Call a POISON CENTER or doctor/ physician if you feel unwell.
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 or doctor/ physician.
P308 + P313 IF exposed or concerned: Get medical advice/ attention.
P332 + P313 If skin irritation occurs: Get medical advice/ attention.
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
May form explosive dust-air mixture during processing, handling or other means.

SECTION 3. COMPOSITION/INFORMATION ON INGREDIENTS

<table>
<thead>
<tr>
<th>Components</th>
<th>Chemical name</th>
<th>CAS-No.</th>
<th>Concentration (% w/w)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Components</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Cellulose</td>
<td>9004-34-6</td>
<td>&gt;= 30 - &lt; 50</td>
</tr>
<tr>
<td></td>
<td>Alendronate</td>
<td>121268-17-5</td>
<td>&gt;= 20 - &lt; 30</td>
</tr>
<tr>
<td></td>
<td>Colecalciferol</td>
<td>67-97-0</td>
<td>&lt; 0.1</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 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. Never give anything by mouth to an unconscious person.

Most important symptoms and effects, both acute and delayed: 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 fire fighting: 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 fire-fighters: In the event of fire, wear self-contained breathing apparatus. Use personal protective equipment.

SECTION 6. ACCIDENTAL RELEASE MEASURES
SAFETY DATA SHEET

Alendronate / Vitamin D Formulation

Version 6.2  Revision Date: 09/13/2019  SDS Number: 22056-00015  Date of last issue: 24.04.2019  Date of first issue: 15.10.2014

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. 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. 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 deowning 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>VLE-PPT</td>
<td>10 mg/m³</td>
<td>NOM-010-STPS-2014</td>
</tr>
<tr>
<td></td>
<td></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>
<tr>
<td>Colecalciferol</td>
<td>67-97-0</td>
<td>TWA</td>
<td>5 µg/m³ (OEB 4)</td>
<td>Internal</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Wipe limit</td>
<td>50 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**
- Material: Chemical-resistant gloves

**Eye protection**
- Remarks: Consider double gloving.
  - 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 facemask 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**
- Material: 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**: off-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**: Not applicable
- **Relative vapor density**: Not applicable
- **Relative density**: No data available
- **Density**: No data available
- **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
Harmful if swallowed.

Product:
Acute oral toxicity: Acute toxicity estimate: 1,965 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

**Colecalciferol:**
Acute oral toxicity: LD50 (Rat, male): 35 mg/kg
Acute inhalation toxicity: Acute toxicity estimate: 0.05 mg/l
  Exposure time: 4 h
  Test atmosphere: dust/mist
  Method: Expert judgment
Acute dermal toxicity: Acute toxicity estimate: 50 mg/kg
  Method: Expert judgment

**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

**Colecalciferol:**
Species: Rabbit
Result: No eye 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
Colecalciferol:
Test Type : Maurer optimisation test
Routes of exposure : Skin contact
Species : Guinea pig
Result : negative

Germ cell mutagenicity
Not classified based on available information.

Components:

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

Genotoxicity in vitro : 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

Colecalciferol:
Genotoxicity in vitro : Test Type: Bacterial reverse mutation assay (AMES)
Method: OECD Test Guideline 471
Result: equivocal

Test Type: In vitro mammalian cell gene mutation test
Method: OECD Test Guideline 476
Result: negative
Test Type: Chromosome aberration test in vitro
Method: OECD Test Guideline 473
Result: negative

Genotoxicity in vivo:
- Test Type: Mammalian erythrocyte micronucleus test (in vivo cytogenetic assay)
  - Species: Rat
  - Application Route: Ingestion
  - Method: OECD Test Guideline 474
  - Result: negative

Test Type: In vivo mammalian alkaline comet assay
- Species: Rat
- Application Route: Ingestion
- Result: positive

Germ cell mutagenicity - Assessment: Weight of evidence does not support classification as a germ cell mutagen.

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.

**Colecalciferol:**
- Routes of exposure: Ingestion
- Target Organs: Kidney, Blood, Bone
- Assessment: Shown to produce significant health effects in animals at concentrations of 10 mg/kg bw or less.
Repeated dose toxicity

**Components:**

**Cellulose:**
- Species: Rat
- NOAEL: >= 9,000 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
- NOAEL: 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

**Colecalciferol:**
- Species: Rat
- NOAEL: 0.06 mg/kg
- LOAEL: 0.3 mg/kg
- Application Route: Ingestion
- Exposure time: 90 Days
- Method: OECD Test Guideline 408

**Aspiration toxicity**
Not classified based on available information.

**Components:**

**Alendronate:**
Not applicable

**Experience with human exposure**

**Components:**

**Alendronate:**
- Inhalation: Symptoms: respiratory tract irritation
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SECTION 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 (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

**Colecalciferol:**
Toxicity to fish:
LL50 (Danio rerio (zebra fish)): > 100 mg/l
Exposure time: 96 h
Method: OECD Test Guideline 203
Toxicity to daphnia and other aquatic invertebrates:
- EL50 (Daphnia magna (Water flea)): > 100 mg/l
  - Exposure time: 48 h
  - Method: OECD Test Guideline 202

Toxicity to algae/aquatic plants:
- EL50 (Scenedesmus capricornutum (fresh water algae)): > 100 mg/l
  - Exposure time: 96 h
  - Method: OECD Test Guideline 201

**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

**Colecalciferol:**
- Biodegradability: Result: Not readily biodegradable.
  - Biodegradation: <= 7 %
  - Exposure time: 28 d
  - Method: OECD Test Guideline 301C

**Bioaccumulative potential**

**Components:**

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

**Colecalciferol:**
- Partition coefficient: n-octanol/water: log Pow: > 6.2
  - Method: OECD Test Guideline 107

**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

NOM-002-SCT
Not regulated as a dangerous good

Special precautions for user
Not applicable

SECTION 15. REGULATORY INFORMATION

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

Federal Law for the control of chemical precursors, essential chemical products and machinery for producing capsules, tablets and pills.
Not applicable

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

AICS : not determined
DSL : not determined
IECSC : not determined

SECTION 16. OTHER INFORMATION

Full text of other abbreviations

ACGIH : USA. ACGIH Threshold Limit Values (TLV)
NOM-010-STPS-2014 : Mexico. Norm NOM-010-STPS-2014 on Chemicals Polluting
SAFETY DATA SHEET

Alendronate / Vitamin D Formulation


Revision Date: 09/13/2019

The information is considered as correct, but not exhaustive, and will be used only as a guide, which is based in the current knowledge of the substance or mixture, and is applicable to proper safety precautions for the product.

MX / Z8