SAFETY DATA SHEET
according to Regulation (EC) No. 1907/2006

Alendronate Solid Formulation

SECTION 1: Identification of the substance/mixture and of the company/undertaking

1.1 Product identifier
   Trade name : Alendronate Solid Formulation

1.2 Relevant identified uses of the substance or mixture and uses advised against
   Use of the Substance/Mixture : Pharmaceutical

1.3 Details of the supplier of the safety data sheet
   Company : MSD
   Innishannon
   County Cork - Ireland
   Telephone : 353 214329300
   Telefax : 908-735-1496
   E-mail address of person responsible for the SDS : EHSDATASTEWARD@msd.com

1.4 Emergency telephone number
   1-908-423-6000

SECTION 2: Hazards identification

2.1 Classification of the substance or mixture

Classification (REGULATION (EC) No 1272/2008)
- 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

H315: Causes skin irritation.
H318: Causes serious eye damage.
H361d: Suspected of damaging the unborn child.
H335: May cause respiratory irritation.
H373: May cause damage to organs through prolonged or repeated exposure.

2.2 Label elements

Labelling (REGULATION (EC) No 1272/2008)
- Hazard pictograms :
- Signal word : Danger
- Hazard statements :
  - 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 through prolonged or repeated exposure.

Precautionary statements:
Prevention:
P201  Obtain special instructions before use.
P260  Do not breathe dust.
P264  Wash skin thoroughly after handling.
P280  Wear protective gloves/ protective clothing/ eye protection/ face protection.

Response:
P304 + P340 + P312  IF INHALED: Remove person to fresh air and keep comfortable for breathing. Call a POISON CENTER/ doctor 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/ doctor.

Hazardous components which must be listed on the label:
Alendronate

2.3 Other hazards
May form explosive dust-air mixture during processing, handling or other means.

SECTION 3: Composition/information on ingredients

3.2 Mixtures

Components

<table>
<thead>
<tr>
<th>Chemical name</th>
<th>CAS-No. EC-No. Index-No. Registration number</th>
<th>Classification</th>
<th>Concentration (% w/w)</th>
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<td>Alendronate</td>
<td>121268-17-5</td>
<td>Acute Tox. 4; H302 Skin Irrit. 2; H315 Eye Dam. 1; H318 Repr. 2; H361d STOT SE 3; H335 STOT RE 2; H373</td>
<td>&gt;= 20 - &lt; 30</td>
</tr>
</tbody>
</table>

For explanation of abbreviations see section 16.

SECTION 4: First aid measures

4.1 Description of 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.
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).

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.

4.2 Most important symptoms and effects, both acute and delayed
Risks: 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.

4.3 Indication of any immediate medical attention and special treatment needed
Treatment: Treat symptomatically and supportively.

SECTION 5: Firefighting measures

5.1 Extinguishing media
Suitable extinguishing media: Water spray
Alcohol-resistant foam
Carbon dioxide (CO2)
Dry chemical

Unsuitable extinguishing media: None known.

5.2 Special hazards arising from the substance or mixture
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.
Alendronate Solid Formulation

Hazardous combustion products: Carbon oxides
Nitrogen oxides (NOx)
Phosphorus compounds
Metal oxides

5.3 Advice for firefighters
Special protective equipment for firefighters: In the event of fire, wear self-contained breathing apparatus. Use personal protective equipment.
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.

SECTION 6: Accidental release measures

6.1 Personal precautions, protective equipment and emergency procedures
Personal precautions: Use personal protective equipment. Follow safe handling advice and personal protective equipment recommendations.

6.2 Environmental precautions
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.

6.3 Methods and material for containment and cleaning up
Methods for 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.

6.4 Reference to other sections
See sections: 7, 8, 11, 12 and 13.
SECTION 7: Handling and storage

7.1 Precautions for safe handling

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 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.

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.

7.2 Conditions for safe storage, including any incompatibilities

Requirements for storage areas and containers: 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.

Advice on common storage: Do not store with the following product types: Strong oxidizing agents

7.3 Specific end use(s)

Specific use(s): No data available

SECTION 8: Exposure controls/personal protection

8.1 Control parameters

Occupational Exposure Limits
Alendronate Solid Formulation

8.2 Exposure controls

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
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 face shield or other full face protection if there is a potential for direct contact to the face with dusts, mists, or aerosols.

Hand protection
Material : Chemical-resistant gloves

Remarks : Consider double gloving.

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.

Respiratory protection : If adequate local exhaust ventilation is not available or exposure assessment demonstrates exposures outside the recommended guidelines, use respiratory protection.
Equipment should conform to I.S. EN 143

Filter type : Particulates type (P)

SECTION 9: Physical and chemical properties

9.1 Information on basic physical and chemical properties
Appearance : powder
Colour : white
Odour : odourless
Odour Threshold : No data available
pH : No data available
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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.
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
Solubility(ies)
  Water solubility: No data available
  Partition coefficient: n-octanol/water: Not applicable
Auto-ignition 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.

9.2 Other information
  Flammability (liquids): No data available
  Particle size: No data available

SECTION 10: Stability and reactivity

10.1 Reactivity
  Not classified as a reactivity hazard.
10.2 Chemical stability
Stable under normal conditions.

10.3 Possibility of hazardous reactions
Hazardous reactions: May form explosive dust-air mixture during processing, handling or other means.
Can react with strong oxidizing agents.

10.4 Conditions to avoid
Conditions to avoid: Heat, flames and sparks.
Avoid dust formation.

10.5 Incompatible materials
Materials to avoid: Oxidizing agents

10.6 Hazardous decomposition products
No hazardous decomposition products are known.

SECTION 11: Toxicological information

11.1 Information on toxicological effects
Information on likely routes of exposure:
- Inhalation
- Skin contact
- Ingestion
- Eye contact

Acute toxicity
Not classified based on available information.

Product:
Acute oral toxicity: Acute toxicity estimate: > 2,000 mg/kg
Method: Calculation method

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
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:
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.
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Components:

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:

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:
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 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:
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
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
Eye contact: Symptoms: Severe irritation
Ingestion: Symptoms: Gastrointestinal disturbance, musculoskeletal pain
SECTION 12: Ecological information

12.1 Toxicity

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: 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

12.2 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
12.3 Bioaccumulative potential

**Components:**

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

12.4 Mobility in soil
No data available

12.5 Results of PBT and vPvB assessment
Not relevant

12.6 Other adverse effects
No data available

SECTION 13: Disposal considerations

13.1 Waste treatment methods

- **Product:**
  Dispose of in accordance with local regulations. According to the European Waste Catalogue, Waste Codes are not product specific, but application specific. Waste codes should be assigned by the user, preferably in discussion with the waste disposal authorities.

- **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

14.1 UN number
Not regulated as a dangerous good

14.2 UN proper shipping name
Not regulated as a dangerous good

14.3 Transport hazard class(es)
Not regulated as a dangerous good

14.4 Packing group
Not regulated as a dangerous good

14.5 Environmental hazards
Not regulated as a dangerous good

14.6 Special precautions for user
Not applicable

14.7 Transport in bulk according to Annex II of Marpol and the IBC Code
Remarks : Not applicable for product as supplied.
SECTION 15: Regulatory information

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

REACH - Restrictions on the manufacture, placing on the market and use of certain dangerous substances, preparations and articles (Annex XVII) : Not applicable
REACH - Candidate List of Substances of Very High Concern for Authorisation (Article 59) : Not applicable
REACH - List of substances subject to authorisation (Annex XIV) : Not applicable
Regulation (EC) No 1005/2009 on substances that deplete the ozone layer : Not applicable
Regulation (EU) 2019/1021 on persistent organic pollutants (recast) : Not applicable
Regulation (EC) No 649/2012 of the European Parliament and the Council concerning the export and import of dangerous chemicals : Not applicable

Other regulations:
Take note of Directive 92/85/EEC regarding maternity protection or stricter national regulations, where applicable.
Take note of Directive 94/33/EC on the protection of young people at work or stricter national regulations, where applicable.

The components of this product are reported in the following inventories:
AICS : not determined
DSL : not determined
IECSC : not determined

15.2 Chemical safety assessment
A Chemical Safety Assessment has not been carried out.

SECTION 16: Other information

Other information : Items where changes have been made to the previous version are highlighted in the body of this document by two vertical lines.

Full text of H-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 through prolonged or repeated exposure.
Full text of other abbreviations

Acute Tox. : Acute toxicity
Eye Dam. : Serious eye damage
Repr. : Reproductive toxicity
Skin Irrit. : Skin irritation
STOT RE : Specific target organ toxicity - repeated exposure
STOT SE : Specific target organ toxicity - single exposure
IE OEL : Ireland. List of Chemical Agents and Occupational Exposure Limit Values - Schedule 1
IE OEL / OELV - 8 hrs (TWA) : Occupational exposure limit value (8-hour reference period)

Further information


Classification of the mixture:

Skin Irrit. 2 : H315
Eye Dam. 1 : H318

Classification procedure:

Calculation method
Alendronate Solid Formulation

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<th>Version</th>
<th>Revision Date:</th>
<th>SDS Number:</th>
<th>Date of last issue:</th>
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<td>23.03.2020</td>
<td>22293-00015</td>
<td>13.09.2019</td>
<td>15.10.2014</td>
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</table>

Repr. 2  H361d  Calculation method
STOT SE 3 H335  Calculation method
STOT RE 2 H373  Calculation method

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.

IE / EN