SECTION 1. PRODUCT AND COMPANY IDENTIFICATION

Product name: Olmesartan / Amlodipine Besylate Formulation

Manufacturer or supplier’s details
Company: MSD
Address: Rua Treze de Maio, 1161
Campinas, São Paulo, Brazil 13106-054
Telephone: 908-740-4000
Emergency telephone: 55 19 3758 2000
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 in accordance with ABNT NBR 14725 Standard
Acute toxicity (Oral): Category 5
Eye irritation: Category 2A
Carcinogenicity (Inhalation): Category 2
Reproductive toxicity: Category 1A
Short-term (acute) aquatic hazard: Category 3
Long-term (chronic) aquatic hazard: Category 3

GHS label elements in accordance with ABNT NBR 14725 Standard
Signal Word: Danger
Hazard Statements: H303 May be harmful if swallowed.
H319 Causes serious eye irritation.
H351 Suspected of causing cancer if inhaled.
H360D May damage the unborn child.
H412 Harmful to aquatic life with long lasting effects.

Precautionary Statements:

**Prevention:**
- P201 Obtain special instructions before use.
- P264 Wash skin thoroughly after handling.
- P273 Avoid release to the environment.
- P280 Wear protective gloves/protective clothing/eye protection/face protection.

**Response:**
- P312 Call a POISON CENTER/doctor if you feel unwell.
- P337 + P313 If eye irritation persists: Get medical advice/attention.

Other hazards which do not result in classification:
Contact with dust can cause mechanical irritation or drying of the skin.
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>
<tr>
<td>Olmesartan</td>
<td>144689-63-4</td>
<td>Acute toxicity (Oral), Eye irritation, Category 4, Category 2B, Reproductive toxicity, Category 1A</td>
<td>&gt;= 10 - &lt; 20</td>
</tr>
<tr>
<td>Amlodipine Besylate</td>
<td>652969-01-2</td>
<td>Acute toxicity (Oral), Eye irritation, Category 4, Category 2A, Short-term (acute) aquatic hazard, Category 2, Long-term (chronic) aquatic hazard, Category 2</td>
<td>&gt;= 5 - &lt; 10</td>
</tr>
<tr>
<td>Titanium dioxide</td>
<td>13463-67-7</td>
<td>Carcinogenicity (Inhalation), Category 2</td>
<td>&gt;= 0,1 - &lt; 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 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: 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.

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 serious eye irritation. Suspected of causing cancer if inhaled. May damage the unborn child. Contact with dust can cause mechanical irritation or drying of the skin.

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

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: Use personal protective equipment.
Follow safe handling advice and personal protective equipment recommendations.

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.

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.

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. 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
SAFETY DATA SHEET

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Conditions for safe storage:
- Keep in properly labeled containers.
- Store locked up.
- Keep tightly closed.
- Store in accordance with the particular national regulations.

Materials to avoid:
- Do not store with the following product types:
  - Strong oxidizing agents
  - Organic peroxides
  - Explosives
  - Gases

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>Olmesartan</td>
<td>144689-63-4</td>
<td>TWA</td>
<td>30 µg/m³ (OEB 3)</td>
<td>Internal</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Wipe limit</td>
<td>300 µg/100 cm²</td>
<td>Internal</td>
</tr>
<tr>
<td>Amlodipine Besylate</td>
<td>652969-01-2</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>100 µg/100 cm²</td>
<td>Internal</td>
</tr>
<tr>
<td>Titanium dioxide</td>
<td>13463-67-7</td>
<td>TWA</td>
<td>10 mg/m³ (Titanium dioxide)</td>
<td>ACGIH</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

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.

SECTION 9. PHYSICAL AND CHEMICAL PROPERTIES

- **Appearance**: powder
- **Color**: No data available
- **Odor**: No data available
- **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
May be harmful if swallowed.

Product:
Acute oral toxicity : Acute toxicity estimate: 3.354 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

Olmesartan:
Acute oral toxicity : LD50 (Rat): > 2.000 mg/kg
                     LD50 (Mouse): > 2.000 mg/kg
                     LD50 (Dog): > 1.500 mg/kg
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Acute inhalation toxicity: Remarks: No data available
Acute dermal toxicity: Remarks: No data available

**Amlodipine Besylate:**
Acute oral toxicity: LD50 (Rat): 393 mg/kg

**Titanium dioxide:**
Acute oral toxicity: LD50 (Rat): > 5,000 mg/kg
Acute inhalation toxicity: LC50 (Rat): > 6,82 mg/l
Exposure time: 4 h
Test atmosphere: dust/mist
Assessment: The substance or mixture has no acute inhalation toxicity

**Skin corrosion/irritation**
Not classified based on available information.

**Components:**

**Olmesartan:**
Remarks: No data available

**Titanium dioxide:**
Species: Rabbit
Result: No skin irritation

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

**Components:**

**Olmesartan:**
Species: Rabbit
Result: Moderate eye irritation
Method: Draize Test

**Amlodipine Besylate:**
Species: Rabbit
Result: Severe irritation

**Titanium dioxide:**
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:

Olmesartan:
Routes of exposure: Skin contact
Remarks: No data available

Titanium dioxide:
Test Type: Local lymph node assay (LLNA)
Routes of exposure: Skin contact
Species: Mouse
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
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

Olmesartan:
Genotoxicity in vitro: Test Type: Bacterial reverse mutation assay (AMES)
Result: negative
Test Type: Mutagenicity (in vitro mammalian cytogenetic test)
Result: negative
Test Type: Chromosome aberration test in vitro
Test system: Chinese hamster lung cells
Result: positive
Test Type: Mouse Lymphoma
Result: negative

Genotoxicity in vivo: Test Type: Micronucleus test
Species: Mouse
Cell type: Bone marrow
Application Route: Oral
Result: negative
Germ cell mutagenicity - Assessment : Weight of evidence does not support classification as a germ cell mutagen.

**Amlodipine Besylate:**
Genotoxicity in vitro : Test Type: Bacterial reverse mutation assay (AMES)
Result: negative
Test Type: Chromosome aberration test in vitro
Result: negative

**Titanium dioxide:**
Genotoxicity in vitro : Test Type: Bacterial reverse mutation assay (AMES)
Result: negative
Genotoxicity in vivo : Test Type: In vivo micronucleus test
Species: Mouse
Result: negative

**Carcinogenicity**
Suspected of causing cancer if inhaled.

**Components:**

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

**Olmesartan:**
Species : Rat
Application Route : Oral
Exposure time : 2 Years
Result : negative
Species : Mouse
Application Route : Oral
Exposure time : 6 Months
Result : negative

**Amlodipine Besylate:**
Species : Mouse
Application Route : Oral
Exposure time : 2 Years
Result : negative
Species : Rat
Application Route : Oral
Exposure time : 2 Years
Result : negative
Titanium dioxide:
Species: Rat
Application Route: inhalation (dust/mist/fume)
Exposure time: 2 Years
Method: OECD Test Guideline 453
Result: positive
Remarks: The mechanism or mode of action may not be relevant in humans.

Carcinogenicity - Assessment: Limited evidence of carcinogenicity in inhalation studies with animals.

Reproductive toxicity
May damage 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

Olmesartan:
Effects on fertility: Test Type: Fertility
Species: Rat
Application Route: Oral
Fertility: NOAEL: 1.000 mg/kg body weight
Result: No effects on fertility.

Effects on fetal development: Test Type: Development
Species: Rat
Application Route: Oral
Dose: 1000 milligram per kilogram
Result: No teratogenic effects.

Test Type: Development
Species: Rabbit
Application Route: Oral
Dose: 1 milligram per kilogram
Result: No teratogenic effects.

Test Type: Development
Species: Rat
Application Route: Oral
Developmental Toxicity: LOAEL: >= 1,6 mg/kg body weight
Symptoms: Malformations were observed., Reduced body weight
Result: Effects on postnatal development.
Reproductive toxicity - Assessment: Positive evidence of adverse effects on development from human epidemiological studies.

**Amlodipine Besylate:**

- **Effects on fertility**
  - Test Type: Fertility/early embryonic development
  - Species: Rat
  - Application Route: Ingestion
  - Fertility: NOAEL: 10 mg/kg body weight
  - Result: No effects on fertility.

  - Test Type: Fertility/early embryonic development
  - Species: Rabbit
  - Application Route: Ingestion
  - Fertility: NOAEL: 25 mg/kg body weight
  - Result: No effects on fertility.

- **Effects on fetal development**
  - Test Type: Embryo-fetal development
  - Species: Rat
  - Application Route: Ingestion
  - Developmental Toxicity: LOAEL: 10 mg/kg body weight
  - Result: Effects on fetal development.

  - Test Type: Embryo-fetal development
  - Species: Rabbit
  - Application Route: Ingestion
  - Developmental Toxicity: NOAEL: 10 mg/kg body weight
  - Result: No effects on fetal development.

  - Test Type: Embryo-fetal development
  - Species: Mouse
  - Application Route: Ingestion
  - Developmental Toxicity: LOAEL: 1,6 mg/kg body weight
  - Result: Effects on fetal development.

  Remarks: Maternal toxicity observed.

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

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

**Repeated dose toxicity**

**Components:**

**Cellulose:**
- Species: Rat
- NOAEL: >= 9.000 mg/kg
- Application Route: Ingestion
- Exposure time: 90 Days

**Olmesartan:**
- Species: Rat
NOAEL: 2.000 mg/kg
Application Route: Oral
Exposure time: 24 Months
Remarks: No significant adverse effects were reported

Amlodipine Besylate:
Species: Rat
NOAEL: 15 mg/kg
Application Route: Oral
Exposure time: 90 d
Remarks: No significant adverse effects were reported

Titanium dioxide:
Species: Rat
NOAEL: 24.000 mg/kg
Application Route: Ingestion
Exposure time: 28 Days

Aspiration toxicity
Not classified based on available information.

Experience with human exposure

Product:
Ingestion: Symptoms: Fatigue, Dizziness, Headache, Nausea

Components:

Olmesartan:
Eye contact: Symptoms: Eye irritation
Ingestion: Symptoms: hypotension
Remarks: May cause harm to the unborn child.
Based on Human Evidence

Amlodipine Besylate:
Eye contact: Symptoms: Severe irritation
Ingestion: Symptoms: Nausea, Abdominal pain, Fatigue, Headache, Edema, Palpitation

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
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Version 3.2  
Revision Date: 09/13/2019  
SDS Number: 402525-00010  
Date of last issue: 24.04.2019  
Date of first issue: 07.01.2016

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### Amlodipine Besylate:

**Toxicity to fish**
- LC50 (Pimephales promelas (fathead minnow)): 2.7 mg/l  
  Exposure time: 96 h

**Toxicity to daphnia and other aquatic invertebrates**
- EC50 (Daphnia magna (Water flea)): 3.2 mg/l  
  Exposure time: 48 h

**Toxicity to algae/aquatic plants**
- IC50 (Pseudokirchneriella subcapitata (green algae)): 5.6 mg/l  
  Exposure time: 72 h  
  Method: OECD Test Guideline 201

### Titanium dioxide:

**Toxicity to fish**
- LC50 (Oncorhynchus mykiss (rainbow trout)): > 100 mg/l  
  Exposure time: 96 h  
  Method: OECD Test Guideline 203

**Toxicity to daphnia and other aquatic invertebrates**
- EC50 (Daphnia magna (Water flea)): > 100 mg/l  
  Exposure time: 48 h

**Toxicity to algae/aquatic plants**
- EC50 (Skeletonema costatum (marine diatom)): > 10,000 mg/l  
  Exposure time: 72 h

**Toxicity to microorganisms**
- EC50: > 1,000 mg/l  
  Exposure time: 3 h  
  Method: OECD Test Guideline 209

### Persistence and degradability

**Components:**

**Cellulose:**
- Biodegradability: Result: Readily biodegradable.

### Bioaccumulative potential

**Components:**

**Amlodipine Besylate:**
- Partition coefficient: n-octanol/water: log Pow: 3

**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
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Date of first issue: 07.01.2016

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)

Group 2B: Possibly carcinogenic to humans
Titanium dioxide 13463-67-7

Brazil. Ordinance No. 1274 on the control and monitoring of chemicals. : Not applicable

International Regulations

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

AICS : not determined

DSL : not determined

IECSC : not determined

SECTION 16. OTHER INFORMATION

Further information

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.

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