SAFETY DATA SHEET

Olmesartan / Amlodipine Besylate Formulation

Version 2.4  Revision Date: 10.10.2020  SDS Number: 443865-00012  Date of last issue: 23.03.2020  Date of first issue: 07.01.2016

1. PRODUCT AND COMPANY IDENTIFICATION

Product name: Olmesartan / Amlodipine Besylate Formulation

Manufacturer or supplier’s details
Company: Organon & Co.
Address: 30 Hudson Street, 33nd floor
Jersey City, New Jersey, U.S.A 07302
Telephone: 551-430-6000
Emergency telephone number: 215-631-6999
E-mail address: EHSSTEWARD@organon.com

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

2. HAZARDS IDENTIFICATION

Manufacture, Storage and Import of Hazardous Chemicals Rules 1989

Classification
Not classified as hazardous according to criteria laid down in Part I of Schedule-1.

GHS Classification
Acute toxicity (Oral): Category 5
Serious eye damage/eye irritation: Category 2A
Reproductive toxicity: Category 1A
Short-term (acute) aquatic hazard: Category 3
Long-term (chronic) aquatic hazard: Category 3

GHS label elements
Hazard pictograms:
Signal word: Danger
Hazard statements:
H303 May be harmful if swallowed.
H319 Causes serious eye irritation.
H360D May damage the unborn child.
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H412 Harmful to aquatic life with long lasting effects.

Precautionary statements:

Prevention:
P203 Obtain, read and follow all safety 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:
P301 + P337 + P317 IF SWALLOWED or if eye irritation persists: Get medical help.
P305 + P351 + P338 IF IN EYES: Rinse cautiously with water for several minutes. Remove contact lenses, if present and easy to do. Continue rinsing.
P318 IF exposed or concerned, get medical advice.

Storage:
P405 Store locked up.

Disposal:
P501 Dispose of contents/ container to an approved waste disposal plant.

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.

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>Cellulose</td>
<td>9004-34-6</td>
<td>&gt;= 30 - &lt; 50</td>
</tr>
<tr>
<td>Olmesartan</td>
<td>144689-63-4</td>
<td>&gt;= 10 - &lt; 20</td>
</tr>
<tr>
<td>Amlodipine Besylate</td>
<td>652969-01-2</td>
<td>&gt;= 5 - &lt; 10</td>
</tr>
<tr>
<td>Titanium dioxide</td>
<td>13463-67-7</td>
<td>&gt;= 0.1 - &lt; 1</td>
</tr>
</tbody>
</table>

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.
- 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.

### 5. FIREFIGHTING 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

**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 firefighters**
- In the event of fire, wear self-contained breathing apparatus.
- Use personal protective equipment.

### 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.

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.
- 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.

Conditions for safe storage:
- Keep in properly labelled 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

8. EXPOSURE CONTROLS/PERSONAL PROTECTION

Components 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>
</tbody>
</table>
9. PHYSICAL AND CHEMICAL PROPERTIES

Appearance : powder

Colour : No data available

Odour : No data available
Odour 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
Vapour pressure : Not applicable
Relative vapour 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
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.
Particle size : No data available

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.
Incompatible materials: Oxidizing agents
Hazardous decomposition products: No hazardous decomposition products are known.

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

**Olmesartan:**
Acute oral toxicity: LD50 (Rat): > 2,000 mg/kg
LD50 (Mouse): > 2,000 mg/kg
LD50 (Dog): > 1,500 mg/kg

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

<table>
<thead>
<tr>
<th>Exposure time</th>
<th>Test atmosphere</th>
<th>Assessment</th>
</tr>
</thead>
<tbody>
<tr>
<td>4 h</td>
<td>dust/mist</td>
<td>The substance or mixture has no acute inhalation toxicity</td>
</tr>
</tbody>
</table>

#### 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
- **Method**: Draize Test
- **Result**: Moderate eye irritation

#### Amlodipine Besylate:

- **Species**: Rabbit
- **Result**: Severe irritation

#### Titanium dioxide:

- **Species**: Rabbit
- **Result**: No eye irritation

### Respiratory or skin sensitisation

#### Skin sensitisation

Not classified based on available information.

### Respiratory sensitisation

Not classified based on available information.

### Components:

#### Olmesartan:

- **Exposure routes**: Skin contact
- **Remarks**: No data available

#### Titanium dioxide:
## 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
Not classified based on available information.

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

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

Test Type: Embryo-foetal development  
Species: Mouse  
Application Route: Ingestion  
Developmental Toxicity: LOAEL: 1.6 mg/kg body weight  
Result: Effects on foetal 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

Species: Rat
NOAEL: 10 mg/m³
Application Route: inhalation (dust/mist/fume)
Exposure time: 2 yr

**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, Oedema, Palpitation

**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

**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: IC₅₀ (Pseudokirchneriella subcapitata (green algae)): 5.6
Titanium dioxide:
Toxicity to fish: LC50 (Oncorhynchus mykiss (rainbow trout)): > 100 mg/l
Exposure time: 96 h
Method: OECD Test Guideline 201

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

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.

14. TRANSPORT INFORMATION

International Regulations
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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 IMO instruments
Not applicable for product as supplied.

15. REGULATORY INFORMATION

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

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

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

16. OTHER INFORMATION

Further information

Date format : dd.mm.yyyy

Full text of other abbreviations
ACGIH : USA. ACGIH Threshold Limit Values (TLV)

ACGIH / TWA : 8-hour, time-weighted average

AICL - 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; 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 Development; OPPTS - Office of Chemical Safety and Pollution Prevention; PBT - Persistent, Bioaccumulative and Toxic substance; PICCS - 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.

IN / EN