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

Olmesartan / Amlodipine Besylate Formulation

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

1.1 Product identifier
  Trade name : Olmesartan / Amlodipine Besylate 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
  Shotton Lane
  NE23 3JU Cramlington NU - Great Britain
  Telephone : 44 1 670 59 30 00
  Telefax : 908-735-1496
  E-mail address of person responsible for the SDS : EHSDATASEWARD@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)
  Eye irritation, Category 2 \ H319: Causes serious eye irritation.
  Reproductive toxicity, Category 1A \ H360D: May damage the unborn child.
  Long-term (chronic) aquatic hazard, Category 3 \ H412: Harmful to aquatic life with long lasting effects.

2.2 Label elements

Labelling (REGULATION (EC) No 1272/2008)
  Hazard pictograms :

  Signal word : Danger
  Hazard statements :
    H319 Causes serious eye irritation.
    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:
P308 + P313 IF exposed or concerned: Get medical advice/ attention.
P337 + P313 If eye irritation persists: Get medical advice/ attention.

Hazardous components which must be listed on the label:
Olmesartan

2.3 Other hazards
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

3.2 Mixtures

<table>
<thead>
<tr>
<th>Components</th>
<th>CAS-No.</th>
<th>EC-No.</th>
<th>Index-No.</th>
<th>Registration number</th>
<th>Classification</th>
<th>Concentration (% w/w)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Olmesartan</td>
<td>144689-63-4</td>
<td></td>
<td></td>
<td></td>
<td>Acute Tox.4; H302 Eye Irrit.2; H319 Repr.1A; H360D</td>
<td>&gt;= 10 - &lt; 20</td>
</tr>
<tr>
<td>Amlodipine Besylate</td>
<td>652969-01-2</td>
<td></td>
<td></td>
<td></td>
<td>Acute Tox.4; H302 Eye Irrit.2; H319 Aquatic Chronic2; H411</td>
<td>&gt;= 2.5 - &lt; 10</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 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.

4.2 Most important symptoms and effects, both acute and delayed
Risks: Causes serious eye irritation. May damage the unborn child. Contact with dust can cause mechanical irritation or drying of the skin.

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.

Hazardous combustion products: Carbon 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.
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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 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. Store in accordance with the particular national regulations.

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

7.3 Specific end use(s)
Specific use(s):
No data available

SECTION 8: Exposure controls/personal protection

8.1 Control parameters

<table>
<thead>
<tr>
<th>Components</th>
<th>CAS-No.</th>
<th>Value type (Form of exposure)</th>
<th>Control parameters</th>
<th>Basis</th>
</tr>
</thead>
<tbody>
<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>
</tbody>
</table>
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 faceshield 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.

Filter type:
- Particulates type (P)

SECTION 9: Physical and chemical properties

9.1 Information on basic 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.
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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.

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
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:
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

Skin corrosion/irritation
Not classified based on available information.

Components:
Olmesartan:
Remarks: No data available

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

**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

**Germ cell mutagenicity**
Not classified based on available information.

**Components:**

**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: 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
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Test Type: Chromosome aberration test in vitro
Result: negative

Carcinogenicity
Not classified based on available information.

Components:

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

Reproductive toxicity
May damage the unborn child.

Components:

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
<table>
<thead>
<tr>
<th>Reproductive toxicity - Assessment</th>
<th>Amlodipine Besylate:</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Effects on fertility</strong></td>
<td>Test Type: Fertility/early embryonic development</td>
</tr>
<tr>
<td></td>
<td>Species: Rat</td>
</tr>
<tr>
<td></td>
<td>Application Route: Ingestion</td>
</tr>
<tr>
<td></td>
<td>Fertility: NOAEL: 10 mg/kg body weight</td>
</tr>
<tr>
<td></td>
<td>Result: No effects on fertility</td>
</tr>
<tr>
<td></td>
<td>Test Type: Fertility/early embryonic development</td>
</tr>
<tr>
<td></td>
<td>Species: Rabbit</td>
</tr>
<tr>
<td></td>
<td>Application Route: Ingestion</td>
</tr>
<tr>
<td></td>
<td>Fertility: NOAEL: 25 mg/kg body weight</td>
</tr>
<tr>
<td></td>
<td>Result: No effects on fertility</td>
</tr>
<tr>
<td><strong>Effects on foetal development</strong></td>
<td>Test Type: Embryo-foetal development</td>
</tr>
<tr>
<td></td>
<td>Species: Rat</td>
</tr>
<tr>
<td></td>
<td>Application Route: Ingestion</td>
</tr>
<tr>
<td></td>
<td>Developmental Toxicity: LOAEL: 10 mg/kg body weight</td>
</tr>
<tr>
<td></td>
<td>Result: Effects on foetal development</td>
</tr>
<tr>
<td></td>
<td>Test Type: Embryo-foetal development</td>
</tr>
<tr>
<td></td>
<td>Species: Rabbit</td>
</tr>
<tr>
<td></td>
<td>Application Route: Ingestion</td>
</tr>
<tr>
<td></td>
<td>Developmental Toxicity: NOAEL: 10 mg/kg body weight</td>
</tr>
<tr>
<td></td>
<td>Result: No effects on foetal development</td>
</tr>
<tr>
<td></td>
<td>Test Type: Embryo-foetal development</td>
</tr>
<tr>
<td></td>
<td>Species: Mouse</td>
</tr>
<tr>
<td></td>
<td>Application Route: Ingestion</td>
</tr>
<tr>
<td></td>
<td>Developmental Toxicity: LOAEL: 1.6 mg/kg body weight</td>
</tr>
<tr>
<td></td>
<td>Result: Effects on foetal development</td>
</tr>
<tr>
<td></td>
<td>Remarks: Maternal toxicity observed.</td>
</tr>
</tbody>
</table>

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

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

Components:

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

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

SECTION 12: Ecological information

12.1 Toxicity

Components:

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
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Date of first issue: 07.01.2016

Method: OECD Test Guideline 201

12.2 Persistence and degradability
No data available

12.3 Bioaccumulative potential

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

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
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 (EC) No 850/2004 on persistent organic pollutants : 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.
Young people under the age of 18 are not allowed to use or be exposed to the product professionally. Young people above the age of 15 are, however, except from this rule if the product is a necessary part of their education.

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.
H319 : Causes serious eye irritation.
H360D : May damage the unborn child.
H411 : Toxic to aquatic life with long lasting effects.
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<table>
<thead>
<tr>
<th>Version</th>
<th>Revision Date</th>
<th>SDS Number</th>
<th>Date of last issue</th>
<th>Date of first issue</th>
</tr>
</thead>
</table>

### Full text of other abbreviations

- **Acute Tox.** : Acute toxicity
- **Aquatic Chronic** : Long-term (chronic) aquatic hazard
- **Eye Irrit.** : Eye irritation
- **Repr.** : Reproductive toxicity

### Classification of the mixture:

<table>
<thead>
<tr>
<th>Property</th>
<th>Classification</th>
<th>Procedure</th>
</tr>
</thead>
<tbody>
<tr>
<td>Eye Irrit. 2</td>
<td>H319</td>
<td>Calculation method</td>
</tr>
<tr>
<td>Repr. 1A</td>
<td>H360D</td>
<td>Calculation method</td>
</tr>
<tr>
<td>Aquatic Chronic 3</td>
<td>H412</td>
<td>Calculation method</td>
</tr>
</tbody>
</table>

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.

NO / EN