1. PRODUCT AND COMPANY IDENTIFICATION

Product name: Olmesartan / Amlodipine Besylate Formulation

Manufacturer or supplier’s details
Company: MSD
Address: 50 Tuas West Drive
          Singapore - Singapore 638408
Telephone: 908-740-4000
Emergency telephone number: 65 6697 2111 (24/7/365)
E-mail address: EHSDATASTEWARD@msd.com
Telefax: 908-735-1496

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

2. HAZARDS IDENTIFICATION

GHS Classification
Serious eye damage/eye irritation: Category 2
Reproductive toxicity: Category 1A

GHS label elements
Hazard pictograms: (images)
Signal word: Danger
Hazard statements: H319 Causes serious eye irritation.
                   H360D May damage the unborn child.
Precautionary statements: Prevention:
                          P201 Obtain special instructions before use.
                          P202 Do not handle until all safety precautions have been read
                          and understood.
                          P264 Wash skin thoroughly after handling.
                          P280 Wear protective gloves/protective clothing/eye protec-
                          tion/face protection.
Response:
             P305 + P351 + P338 IF IN EYES: Rinse cautiously with water
             for several minutes. Remove contact lenses, if present and
SAFETY DATA SHEET

Olmesartan / Amlodipine Besylate Formulation

Version     Revision Date:     SDS Number:     Date of last issue:     Date of first issue:

easy to do. Continue rinsing.
P308 + P313 IF exposed or concerned: Get medical advice/ attention.
P337 + P313 If eye irritation persists: Get medical advice/ attention.

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

<table>
<thead>
<tr>
<th>Substance / Mixture</th>
<th>Components</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>CAS-No.</td>
</tr>
<tr>
<td>Cellulose</td>
<td>9004-34-6</td>
</tr>
<tr>
<td>Olmesartan</td>
<td>144689-63-4</td>
</tr>
<tr>
<td>Amlodipine Besylate</td>
<td>652969-01-2</td>
</tr>
<tr>
<td>Titanium dioxide</td>
<td>13463-67-7</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: 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 and personal protective equipment recommendations.

Environmental precautions: Discharge into the environment must be avoided. Prevent further leakage or spillage if safe to do so. Retain and dispose of contaminated wash water. Local authorities should be advised if significant spillages cannot be contained.

Methods and materials for containment and cleaning up: Sweep up or vacuum up spillage and collect in suitable container for disposal. Avoid dispersal of dust in the air (i.e., clearing dust surfaces with compressed air). Dust deposits should not be allowed to accumulate on surfaces, as these may form an explosive mixture if they are released into the atmosphere in sufficient concentration. Local or national regulations may apply to releases and disposal of this material, as well as those materials and items employed in the cleanup of releases. You will need to determine which regulations are applicable. Sections 13 and 15 of this SDS provide information regarding certain local or national requirements.
7. HANDLING AND STORAGE

Technical measures: Static electricity may accumulate and ignite suspended dust causing an explosion. Provide adequate precautions, such as electrical grounding and bonding, or inert atmospheres.

Local/Total ventilation: If sufficient ventilation is unavailable, use with local exhaust ventilation.

Advice on safe handling: Do not get on skin or clothing. Do not breathe dust. Do not swallow. Do not get in eyes. Handle in accordance with good industrial hygiene and safety practice, based on the results of the workplace exposure assessment. Keep container tightly closed. 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>PEL (long term)</td>
<td>10 mg/m³</td>
<td>SG OEL</td>
</tr>
<tr>
<td></td>
<td></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>PEL (long term)</td>
<td>10 mg/m³</td>
<td>SG OEL</td>
</tr>
<tr>
<td></td>
<td></td>
<td>TWA</td>
<td>10 mg/m³</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
- **Material**: Chemical-resistant gloves

#### 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.

#### 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.

### 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**: No data available
SAFETY DATA SHEET

Olmesartan / Amlodipine Besylate Formulation

Version 2.8
Revision Date: 09/13/2019
SDS Number: 402652-00010
Date of last issue: 24.04.2019
Date of first issue: 07.01.2016

range
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.
Avoid dust formation.
Incompatible materials : Oxidizing agents
11. TOXICOLOGICAL INFORMATION

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:

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
- 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 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:**
Test Type: Local lymph node assay (LLNA)
Exposure routes: Skin contact
Species: Mouse
Result: negative
SAFETY DATA SHEET

Olmesartan / Amlodipine Besylate Formulation

Version 2.8 Revision Date: 09/13/2019 SDS Number: 402652-00010 Date of last issue: 24.04.2019
Date of first issue: 07.01.2016

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
## 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 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 foetal development**
  - Test Type: Fertility/early embryonic development
  - Species: Rat
  - Application Route: Ingestion
  - Result: negative

#### Olmesartan:
- **Effects on fertility**
  - Test Type: Fertility
  - 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
  - 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 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

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

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.

15. REGULATORY INFORMATION

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

Workplace Safety and Health Act and Workplace Safety and Health (General Provisions) Regulations: This product is subjected to the SDS, labelling, PEL and other requirements in the Act/Regulations.

- Environmental Protection and Management Act and Environmental Protection and Management (Hazardous Substances) Regulations: Not applicable
- Fire Safety (Petroleum and Flammable Materials) Regulations: Not applicable

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
Sources of key data used to compile the Safety Data Sheet:
- Date format: dd.mm.yyyy

Full text of other abbreviations

- ACGIH: USA, ACGIH Threshold Limit Values (TLV)
- SG OEL: Singapore, Workplace Safety and Health Act - First Schedule Permissible Exposure Limits of Toxic Substances
- ACGIH / TWA: 8-hour, time-weighted average
- SG OEL / PEL (long term): Permissible Exposure Level (PEL) Long Term
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.

SG / EN