SAFETY DATA SHEET

Olmesartan / Hydrochlorothiazide Formulation

Version 3.8  Revision Date: 10.10.2020  SDS Number: 402623-00012  Date of last issue: 23.03.2020

1. PRODUCT AND COMPANY IDENTIFICATION

Product name: Olmesartan / Hydrochlorothiazide 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

GHS Classification

Reproductive toxicity: Category 1A
Specific target organ toxicity - repeated exposure: Category 2 (Kidney, Parathyroid gland)

GHS label elements

Hazard pictograms:

Signal word: Danger
Hazard statements: H360D May damage the unborn child.
                  H373 May cause damage to organs (Kidney, Parathyroid gland) through prolonged or repeated exposure.

Precautionary statements:
Prevention:
P201 Obtain special instructions before use.
P202 Do not handle until all safety precautions have been read and understood.
P260 Do not breathe dust.
P280 Wear protective gloves/ protective clothing/ eye protection/ face protection.

Response:
P308 + P313 IF exposed or concerned: 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
Dust contact with the eyes can lead to mechanical irritation.
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>Olmesartan</td>
<td>CAS-No. 144689-63-4, Concentration &gt;=1 - &lt; 10</td>
</tr>
<tr>
<td>Cellulose</td>
<td>CAS-No. 9004-34-6, Concentration &gt;=1 - &lt; 10</td>
</tr>
<tr>
<td>Hydrochlorothiazide</td>
<td>CAS-No. 58-93-5, Concentration &gt;=1 - &lt; 10</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: 
If in eyes, rinse well with water.
Get medical attention if irritation develops and persists.

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 damage the unborn child.
May cause damage to organs through prolonged or repeated exposure.
Contact with dust can cause mechanical irritation or drying of the skin.
Dust contact with the eyes can lead to mechanical irritation.

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
Nitrogen oxides (NOx)
Chlorine compounds
Sulphur 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. Avoid contact with 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. Do not eat, drink or smoke when using this product. 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>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>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>Hydrochlorothiazide</td>
<td>58-93-5</td>
<td>TWA</td>
<td>100 µg/m³ (OEB 2)</td>
<td>Internal</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: 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.

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: white to off-white

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, han-
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.

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:**

**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

**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

**Hydrochlorothiazide:**
Acute oral toxicity:
- LD50 (Rat): > 2,750 mg/kg
- LD50 (Mouse): > 2,830 mg/kg

Acute toxicity (other routes of administration):
- LD50 (Rat): 990 mg/kg
  Application Route: Intravenous
- LD50 (Mouse): 590 mg/kg
  Application Route: Intravenous

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

**Components:**

**Olmesartan:**
Remarks:
- No data available
Hydrochlorothiazide:
Species : Rabbit
Result : No skin irritation

Serious eye damage/eye irritation
Not classified based on available information.

Components:

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

Hydrochlorothiazide:
Species : Rabbit
Result : Mild 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

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 -  
Assessment  
: Weight of evidence does not support classification as a germ cell mutagen.

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

Hydrochlorothiazide:  
Genotoxicity in vitro  
: Test Type: Bacterial reverse mutation assay (AMES)  
Result: negative  

Test Type: Chromosomal aberration  
Test system: Chinese hamster ovary cells  
Result: negative  

Test Type: sister chromatid exchange assay  
Test system: Chinese hamster ovary cells  
Result: positive  

Test Type: in vitro assay  
Test system: mouse lymphoma cells  
Result: positive  

Genotoxicity in vivo  
: Test Type: Chromosomal aberration  
Species: Chinese hamster  
Cell type: Bone marrow  
Result: negative  

Test Type: in vivo assay  
Species: Mouse  
Cell type: Bone marrow  
Result: negative  

Germ cell mutagenicity -  
Assessment  
: Weight of evidence does not support classification as a germ cell mutagen.

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

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

Hydrochlorothiazide:
Species: Mouse, female
Application Route: Oral
Exposure time: 2 Years
Result: negative

Species: Mouse, male
Application Route: Oral
Exposure time: 2 Years
Result: equivocal

Species: Rat, male and female
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  
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.

**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

**Hydrochlorothiazide:**  
Effects on fertility:  
Test Type: Fertility  
Species: Rat, male and female  
Application Route: oral (feed)  
Fertility: NOAEL: 4 mg/kg body weight  
Result: Effects on fertility

Test Type: Fertility  
Species: Mouse, male and female  
Application Route: oral (feed)  
Fertility: NOAEL: 100 mg/kg body weight  
Result: Effects on fertility

Effects on foetal development:  
Test Type: Development  
Species: Mouse  
Application Route: Oral  
Developmental Toxicity: NOAEL: 3,000 mg/kg body weight  
Result: No teratogenic effects

Test Type: Development  
Species: Rat  
Application Route: Oral  
Developmental Toxicity: NOAEL: 1,000 mg/kg body weight  
Result: No teratogenic effects
STOT - single exposure
Not classified based on available information.

STOT - repeated exposure
May cause damage to organs (Kidney, Parathyroid gland) through prolonged or repeated exposure.

Components:

Hydrochlorothiazide:
Target Organs : Kidney, Parathyroid gland
Assessment : Causes damage to organs through prolonged or repeated exposure.

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

Cellulose:
Species : Rat
NOAEL : >= 9,000 mg/kg
Application Route : Ingestion
Exposure time : 90 Days

Hydrochlorothiazide:
Species : Rat, male and female
LOAEL : 10 mg/kg
Application Route : Oral
Exposure time : 2 yr
Target Organs : Kidney, Parathyroid gland

Species : Mouse, male and female
NOAEL : 300 - 550 mg/kg
Application Route : Oral
Exposure time : 2 yr
Remarks : No significant adverse effects were reported

Species : Dog
Application Route : Oral
Exposure time : 9 Months
Target Organs : Parathyroid gland

Aspiration toxicity
Not classified based on available information.
Components:

Hydrochlorothiazide:
No aspiration toxicity classification

Experience with human exposure

Components:

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

Hydrochlorothiazide:
Eye contact : Symptoms: Eye irritation
Ingestion : Symptoms: Dizziness, Headache, Fatigue, Nausea, Abdominal pain, hypotension, dry mouth, electrolyte imbalance, eye pain

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

Hydrochlorothiazide:
Toxicity to fish : LC50 (Pimephales promelas (fathead minnow)): > 500 mg/l
Exposure time: 96 h

Toxicity to daphnia and other aquatic invertebrates : EC50 (Daphnia magna (Water flea)): > 500 mg/l
Exposure time: 48 h

Persistence and degradability

Components:

Cellulose:
Biodegradability : Result: Readily biodegradable.

Hydrochlorothiazide:
Stability in water : Hydrolysis: 46.2 %(96 h)

Bioaccumulative potential
No data available
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

AliC - 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; 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.

SG / EN