

Olmesartan / Amlodipine Besylate / Hydrochlorothiazide Formulation

Version 1.0 Revision Date: 2019/10/07 SDS Number: 4944960-00001 Date of last issue: -
Date of first issue: 2019/10/07

1. PRODUCT AND COMPANY IDENTIFICATION

Product name : Olmesartan / Amlodipine Besylate / Hydrochlorothiazide Formulation

Manufacturer or supplier's details

Company name of supplier : MSD
Address : Kumagaya, Saitama Prefecture , Xicheng 810 MSD Co., Ltd. Menuma factory
Telephone : 048-588-8411
E-mail address : EHSDATASTEWARD@msd.com
Emergency telephone number : 1-908-423-6000

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
Specific target organ toxicity - repeated exposure : Category 2 (Kidney, Parathyroid gland)
Short-term (acute) aquatic hazard : Category 3
Long-term (chronic) aquatic hazard : Category 3

GHS label elements

Hazard pictograms :  

Signal word : Danger

Hazard statements : H319 Causes serious eye irritation.
H360D May damage the unborn child.
H373 May cause damage to organs (Kidney, Parathyroid gland) through prolonged or repeated exposure.
H412 Harmful to aquatic life with long lasting effects.

Olmesartan / Amlodipine Besylate / Hydrochlorothiazide Formulation

Version 1.0 Revision Date: 2019/10/07 SDS Number: 4944960-00001 Date of last issue: -
Date of first issue: 2019/10/07

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.
 P264 Wash skin thoroughly after handling.
 P273 Avoid release to the environment.
 P280 Wear protective gloves/ protective clothing/ eye protection/ face protection.

Response:
 P305 + P351 + P338 IF IN EYES: Rinse cautiously with water for several minutes. Remove contact lenses, if present and 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

Important symptoms and out- : Contact with dust can cause mechanical irritation or drying of
 lines of the emergency as- the skin.
 sumed May form explosive dust-air mixture during processing, handling or other means.

3. COMPOSITION/INFORMATION ON INGREDIENTS

Substance / Mixture : Mixture

Components

| Chemical name | CAS-No. | Concentration (% w/w) | ENCS No. |
|---------------------|-------------|-----------------------|----------|
| Cellulose | 9004-34-6 | >= 40 - < 50 | |
| Starch | 9005-25-8 | >= 30 - < 40 | 8-98 |
| Olmesartan | 144689-63-4 | >= 10 - < 20 | |
| Hydrochlorothiazide | 58-93-5 | >= 1 - < 10 | |
| Amlodipine Besylate | 652969-01-2 | >= 2.5 - < 10 | |
| Silicon dioxide | 7631-86-9 | >= 0.1 - < 1 | 1-548 |

4. FIRST AID MEASURES

General advice : In the case of accident or if you feel unwell, seek medical ad-

Olmesartan / Amlodipine Besylate / Hydrochlorothiazide Formulation

| | | | |
|----------------|------------------------------|------------------------------|--|
| Version 1.0 | Revision Date: 2019/10/07 | SDS Number: 4944960-00001 | Date of last issue: - Date of first issue: 2019/10/07 |
|----------------|------------------------------|------------------------------|--|

- vice 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.
May cause damage to organs through prolonged or repeated exposure.
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 fire-fighting : Avoid generating dust; fine dust dispersed in air in sufficient concentrations, and in the presence of an ignition source is a potential dust explosion hazard.
Exposure to combustion products may be a hazard to health.
- Hazardous combustion products : Carbon oxides
Nitrogen oxides (NO_x)
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.

Olmesartan / Amlodipine Besylate / Hydrochlorothiazide Formulation

| | | | |
|---------|----------------|---------------|---------------------------------|
| Version | Revision Date: | SDS Number: | Date of last issue: - |
| 1.0 | 2019/10/07 | 4944960-00001 | Date of first issue: 2019/10/07 |

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

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. 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.

Olmesartan / Amlodipine Besylate / Hydrochlorothiazide Formulation

Version 1.0 Revision Date: 2019/10/07 SDS Number: 4944960-00001 Date of last issue: -
Date of first issue: 2019/10/07

Avoidance of contact : Oxidizing agents
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.

Storage

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
Packaging material : Unsuitable material: None known.

8. EXPOSURE CONTROLS/PERSONAL PROTECTION

Threshold limit value and permissible exposure limits for each component in the work environment

| Components | CAS-No. | Value type (Form of exposure) | Control parameters / Permissible concentration | Basis |
|---------------------|-------------|-------------------------------|--|----------|
| Cellulose | 9004-34-6 | TWA | 10 mg/m ³ | ACGIH |
| Starch | 9005-25-8 | TWA | 10 mg/m ³ | ACGIH |
| Olmesartan | 144689-63-4 | TWA | 30 µg/m ³ (OEB 3) | Internal |
| | | Wipe limit | 300 µg/100 cm ² | Internal |
| Hydrochlorothiazide | 58-93-5 | TWA | 100 µg/m ³ (OEB 2) | Internal |
| Amlodipine Besylate | 652969-01-2 | TWA | 20 µg/m ³ (OEB 3) | Internal |
| | | Wipe limit | 100 µg/100 cm ² | Internal |

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

Olmesartan / Amlodipine Besylate / Hydrochlorothiazide Formulation

| | | | |
|----------------|------------------------------|------------------------------|--|
| Version 1.0 | Revision Date: 2019/10/07 | SDS Number: 4944960-00001 | Date of last issue: - Date of first issue: 2019/10/07 |
|----------------|------------------------------|------------------------------|--|

Hand protection

Material : Chemical-resistant gloves

Remarks : Consider double gloving.

Eye protection : Wear safety glasses with side shields or goggles.
If the work environment or activity involves dusty conditions, mists or aerosols, wear the appropriate goggles.
Wear a faceshield or other full face protection if there is a potential for direct contact to the face with dusts, mists, or aerosols.

Skin and body protection : Work uniform or laboratory coat.
Additional body garments should be used based upon the task being performed (e.g., sleevelets, apron, gauntlets, disposable suits) to avoid exposed skin surfaces.
Use appropriate degowning techniques to remove potentially contaminated clothing.

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.

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

Olmesartan / Amlodipine Besylate / Hydrochlorothiazide Formulation

| | | | |
|---------|----------------|---------------|---------------------------------|
| Version | Revision Date: | SDS Number: | Date of last issue: - |
| 1.0 | 2019/10/07 | 4944960-00001 | Date of first issue: 2019/10/07 |

| | | |
|--|---|--|
| 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. |
| Molecular weight | : | No data available |
| 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 |
| 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 |
|---------------------|---|--|

Olmesartan / Amlodipine Besylate / Hydrochlorothiazide Formulation

Version 1.0 Revision Date: 2019/10/07 SDS Number: 4944960-00001 Date of last issue: -
Date of first issue: 2019/10/07

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

Starch:

Acute oral toxicity : LD50 (Mouse): > 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

Hydrochlorothiazide:

Acute oral toxicity : LD50 (Rat): 10,000 mg/kg
LD50 (Mouse): 10,000 mg/kg

Acute toxicity (other routes of administration) : LD50 (Rat): 990 mg/kg
Application Route: Intravenous
LD50 (Dog): 250 mg/kg
Application Route: Intravenous

Amlodipine Besylate:

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

Silicon dioxide:

Acute oral toxicity : LD50 (Rat): > 5,000 mg/kg
Method: OECD Test Guideline 401

Acute inhalation toxicity : LC50 (Rat): > 2.08 mg/l
Exposure time: 4 h
Test atmosphere: dust/mist
Assessment: The substance or mixture has no acute inhalation toxicity

Acute dermal toxicity : LD50 (Rabbit): > 5,000 mg/kg

Olmesartan / Amlodipine Besylate / Hydrochlorothiazide Formulation

Version 1.0 Revision Date: 2019/10/07 SDS Number: 4944960-00001 Date of last issue: -
Date of first issue: 2019/10/07

Skin corrosion/irritation

Not classified based on available information.

Components:**Olmesartan:**

Remarks : No data available

Hydrochlorothiazide:

Species : Rabbit
Result : No skin irritation

Silicon dioxide:

Species : Rabbit
Method : OECD Test Guideline 404
Result : No skin irritation

Serious eye damage/eye irritation

Causes serious eye irritation.

Components:**Olmesartan:**

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

Hydrochlorothiazide:

Species : Rabbit
Result : Mild eye irritation

Amlodipine Besylate:

Species : Rabbit
Result : Severe irritation

Silicon dioxide:

Species : Rabbit
Result : No eye irritation
Method : OECD Test Guideline 405

Respiratory or skin sensitisation**Skin sensitisation**

Not classified based on available information.

Respiratory sensitisation

Not classified based on available information.

Olmesartan / Amlodipine Besylate / Hydrochlorothiazide Formulation

Version 1.0 Revision Date: 2019/10/07 SDS Number: 4944960-00001 Date of last issue: -
Date of first issue: 2019/10/07

Components:**Olmesartan:**

Exposure routes : Skin contact
Remarks : No data available

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.

Hydrochlorothiazide:

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

Test Type: Chromosomal aberration

Olmesartan / Amlodipine Besylate / Hydrochlorothiazide Formulation

| | | | |
|---------|----------------|---------------|---------------------------------|
| Version | Revision Date: | SDS Number: | Date of last issue: - |
| 1.0 | 2019/10/07 | 4944960-00001 | Date of first issue: 2019/10/07 |

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.

Amlodipine Besylate:

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

Test Type: Chromosome aberration test in vitro
Result: negative

Silicon dioxide:

Genotoxicity in vitro : Test Type: Bacterial reverse mutation assay (AMES)
Method: OECD Test Guideline 471
Result: negative

Genotoxicity in vivo : Test Type: Mutagenicity (in vivo mammalian bone-marrow cytogenetic test, chromosomal analysis)
Species: Rat
Application Route: Ingestion
Result: negative

Carcinogenicity

Not classified based on available information.

Components:

Cellulose:

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

Olmesartan / Amlodipine Besylate / Hydrochlorothiazide Formulation

Version 1.0 Revision Date: 2019/10/07 SDS Number: 4944960-00001 Date of last issue: -
Date of first issue: 2019/10/07

Olmesartan:

Species : Rat
Application Route : Oral
Exposure time : 2 Years
Result : negative

Species : Mouse
Application Route : Oral
Exposure time : 6 Months
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

Amlodipine Besylate:

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

Species : Rat
Application Route : Oral
Exposure time : 2 Years
Result : negative

Silicon dioxide:

Species : Rat
Application Route : Ingestion
Exposure time : 103 weeks
Result : negative

Reproductive toxicity

May damage the unborn child.

Components:**Cellulose:**

Olmesartan / Amlodipine Besylate / Hydrochlorothiazide Formulation

| | | | |
|----------------|------------------------------|------------------------------|--|
| Version 1.0 | Revision Date: 2019/10/07 | SDS Number: 4944960-00001 | Date of last issue: - Date of first issue: 2019/10/07 |
|----------------|------------------------------|------------------------------|--|

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: \geq 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.

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

Olmesartan / Amlodipine Besylate / Hydrochlorothiazide Formulation

Version 1.0 Revision Date: 2019/10/07 SDS Number: 4944960-00001 Date of last issue: -
Date of first issue: 2019/10/07

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

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.

Silicon dioxide:

Effects on foetal development : Test Type: Embryo-foetal development
Species: Rat
Application Route: Ingestion
Result: negative

Olmesartan / Amlodipine Besylate / Hydrochlorothiazide Formulation

Version 1.0 Revision Date: 2019/10/07 SDS Number: 4944960-00001 Date of last issue: -
Date of first issue: 2019/10/07

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:****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

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
: 50 - 200 mg/kg
Application Route : Oral
Exposure time : 9 Months
Target Organs : Parathyroid gland

Amlodipine Besylate:

Olmesartan / Amlodipine Besylate / Hydrochlorothiazide Formulation

| | | | |
|---------|----------------|---------------|---------------------------------|
| Version | Revision Date: | SDS Number: | Date of last issue: - |
| 1.0 | 2019/10/07 | 4944960-00001 | Date of first issue: 2019/10/07 |

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

Silicon dioxide:

Species : Rat
NOAEL : 1.3 mg/m³
Application Route : inhalation (dust/mist/fume)
Exposure time : 13 Weeks

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

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

Olmesartan / Amlodipine Besylate / Hydrochlorothiazide Formulation

| | | | |
|---------|----------------|---------------|---------------------------------|
| Version | Revision Date: | SDS Number: | Date of last issue: - |
| 1.0 | 2019/10/07 | 4944960-00001 | Date of first issue: 2019/10/07 |

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

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

Silicon dioxide:

Toxicity to fish : LC50 (Danio rerio (zebra fish)): > 10,000 mg/l
Exposure time: 96 h
Method: OECD Test Guideline 203

Toxicity to daphnia and other aquatic invertebrates : EC50 (Daphnia magna (Water flea)): > 1,000 mg/l
Exposure time: 24 h
Method: OECD Test Guideline 202

Toxicity to algae/aquatic plants : EC50 (Desmodesmus subspicatus (green algae)): > 10,000 mg/l
Exposure time: 72 h
Method: OECD Test Guideline 201
Remarks: Based on data from similar materials

NOEC (Desmodesmus subspicatus (green algae)): 10,000 mg/l
Exposure time: 72 h
Method: OECD Test Guideline 201
Remarks: Based on data from similar materials

Persistence and degradability**Components:****Cellulose:**

Biodegradability : Result: Readily biodegradable.

Hydrochlorothiazide:

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

Olmesartan / Amlodipine Besylate / Hydrochlorothiazide Formulation

Version 1.0 Revision Date: 2019/10/07 SDS Number: 4944960-00001 Date of last issue: -
Date of first issue: 2019/10/07

Bioaccumulative potential**Components:****Amlodipine Besylate:**

Partition coefficient: n-octanol/water : log Pow: 3

Mobility in soil

No data available

Hazardous to the ozone layer

Not applicable

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.

National Regulations

Refer to section 15 for specific national regulation.

15. REGULATORY INFORMATION**Related Regulations****Fire Service Law**

Not applicable to dangerous materials / designated flammables.

Chemical Substance Control Law

Not applicable for Specified Chemical Substance, Monitoring Chemical Substance and Priority Assessment Chemical Substance.

Olmesartan / Amlodipine Besylate / Hydrochlorothiazide Formulation

Version 1.0 Revision Date: 2019/10/07 SDS Number: 4944960-00001 Date of last issue: -
Date of first issue: 2019/10/07

Industrial Safety and Health Law

Harmful Substances Prohibited from Manufacture

Not applicable

Harmful Substances Required Permission for Manufacture

Not applicable

Substances Prevented From Impairment of Health

Not applicable

Circular concerning Information on Chemicals having Mutagenicity - Annex 2: Information on Existing Chemicals having Mutagenicity

Not applicable

Circular concerning Information on Chemicals having Mutagenicity - Annex 1: Information on Notified Substances having Mutagenicity

Not applicable

Substances Subject to be Notified Names

Article 57-2 (Enforcement Order Table 9)

| Chemical name | Number | Concentration (%) |
|--------------------|---------|-------------------|
| Crystalline silica | 165 の 2 | >=0.1 - <1 |

Substances Subject to be Indicated Names

Article 57 (Enforcement Order Article 18)

| Chemical name | Number |
|--------------------|---------|
| Crystalline silica | 165 の 2 |

Ordinance on Prevention of Hazards Due to Specified Chemical Substances

Not applicable

Ordinance on Prevention of Lead Poisoning

Not applicable

Ordinance on Prevention of Tetraalkyl Lead Poisoning

Not applicable

Ordinance on Prevention of Organic Solvent Poisoning

Not applicable

Enforcement Order of the Industrial Safety and Health Law - Attached table 1 (Dangerous Substances)

Not applicable

Poisonous and Deleterious Substances Control Law

Not applicable

Act on Confirmation, etc. of Release Amounts of Specific Chemical Substances in the Environment and Promotion of Improvements to the Management Thereof

Not applicable

High Pressure Gas Safety Act

Not applicable

Olmesartan / Amlodipine Besylate / Hydrochlorothiazide Formulation

Version 1.0 Revision Date: 2019/10/07 SDS Number: 4944960-00001 Date of last issue: -
Date of first issue: 2019/10/07

Explosive Control Law

Not applicable

Vessel Safety Law

Not regulated as a dangerous good

Aviation Law

Not regulated as a dangerous good

Marine Pollution and Sea Disaster Prevention etc Law

Bulk transportation : Not classified as noxious liquid substance

Pack transportation : Not classified as marine pollutant

Narcotics and Psychotropics Control Act

Narcotic or Psychotropic Raw Material (Export / Import Permission)

Not applicable

Specific Narcotic or Psychotropic Raw Material (Export / Import permission)

Not applicable

Waste Disposal and Public Cleansing Law

Industrial waste

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

: not determined

16. OTHER INFORMATION**Further information**Sources of key data used to compile the Safety Data Sheet : Internal technical data, data from raw material SDSs, OECD eChem Portal search results and European Chemicals Agency, <http://echa.europa.eu/>

Date format : yyyy/mm/dd

Full text of other abbreviations

ACGIH : USA. ACGIH Threshold Limit Values (TLV)

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

AICS - Australian Inventory of Chemical Substances; 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

Olmesartan / Amlodipine Besylate / Hydrochlorothiazide Formulation

| | | | |
|---------|----------------|---------------|---------------------------------|
| Version | Revision Date: | SDS Number: | Date of last issue: - |
| 1.0 | 2019/10/07 | 4944960-00001 | Date of first issue: 2019/10/07 |

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.

JP / EN