SAFETY DATA SHEET

Amiloride / Hydrochlorothiazide Formulation

Version 5.1  Revision Date: 01.10.2020  SDS Number: 44137-00014  Date of last issue: 23.03.2020  Date of first issue: 05.01.2015

SECTION 1. PRODUCT AND COMPANY IDENTIFICATION

Product name: Amiloride / Hydrochlorothiazide Formulation

Manufacturer or supplier’s details

Company: MSD
Address: 855 Leandro N. Alem St., 8 Floor  
Buenos Aires, Argentina  C1001AFB
Telephone: 908-740-4000
Emergency telephone: 1-908-423-6000
E-mail address: EHSDATASTEWARD@msd.com
Telefax: 908-735-1496

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

SECTION 2. HAZARDS IDENTIFICATION

GHS Classification
Acute toxicity (Oral): Category 4
Specific target organ toxicity - repeated exposure: Category 1 (Kidney, Parathyroid gland)

GHS label elements

Hazard pictograms:

Signal Word: Danger
Hazard Statements: H302 Harmful if swallowed.  
H372 Causes damage to organs (Kidney, Parathyroid gland) through prolonged or repeated exposure.

Precautionary Statements: Prevention:
P260 Do not breathe dust.  
P264 Wash skin thoroughly after handling.  
P270 Do not eat, drink or smoke when using this product.
Response:
P301 + P312 + P330 IF SWALLOWED: Call a POISON CENTER/ doctor if you feel unwell. Rinse mouth.  
P314 Get medical advice/ attention if you feel unwell.
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.

SECTION 3. COMPOSITION/INFORMATION ON INGREDIENTS

Substance / Mixture : Mixture

Components

<table>
<thead>
<tr>
<th>Chemical name</th>
<th>CAS-No.</th>
<th>Concentration (% w/w)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hydrochlorothiazide</td>
<td>58-93-5</td>
<td>&gt;= 20 - &lt; 30</td>
</tr>
<tr>
<td>Starch</td>
<td>9005-25-8</td>
<td>&gt;= 10 - &lt; 20</td>
</tr>
<tr>
<td>Amiloride</td>
<td>17440-83-4</td>
<td>&gt;= 1 - &lt; 2,5</td>
</tr>
</tbody>
</table>

SECTION 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 if symptoms occur.

In case of skin contact : In case of contact, immediately flush skin with soap and plenty of water.
Get medical attention if symptoms occur.

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 unless directed to do so by medical personnel.
Get medical attention.
Rinse mouth thoroughly with water.
Never give anything by mouth to an unconscious person.

Most important symptoms and effects, both acute and delayed : Harmful if swallowed.
Causes 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.

SECTION 5. FIRE-FIGHTING MEASURES

Suitable extinguishing media : Water spray
Alcohol-resistant foam
SAFETY DATA SHEET

Amiloride / Hydrochlorothiazide Formulation

Unsuitable extinguishing media

Carbon dioxide (CO2)
Dry chemical

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 (NOx)
Chlorine compounds
Sulfur oxides
Metal oxides
Oxides of phosphorus

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 fire-fighters

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

SECTION 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.

SECTION 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: Use only with adequate ventilation.

Advice on safe handling:
- Do not breathe dust.
- Do not swallow.
- Avoid contact with eyes.
- Avoid prolonged or repeated contact with skin.
- Wash skin thoroughly after handling.
- Handle in accordance with good industrial hygiene and safety practice, based on the results of the workplace exposure assessment.
- 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 labeled containers.
- Store in accordance with the particular national regulations.

Materials to avoid:
- Do not store with the following product types:
  - Strong oxidizing agents
  - Organic peroxides
  - Explosives
  - Gases

SECTION 8. EXPOSURE CONTROLS/PERSONAL PROTECTION

Ingredients 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>Hydrochlorothiazide</td>
<td>58-93-5</td>
<td>TWA</td>
<td>100 µg/m³ (OEL 2)</td>
<td>Internal</td>
</tr>
<tr>
<td>Starch</td>
<td>9005-25-8</td>
<td>CMP</td>
<td>10 mg/m³</td>
<td>AR OEL</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Further information: A4 - Not classifiable as a human carcinogen, lung, Dermatitis</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>TWA</td>
<td>10 mg/m³</td>
<td>ACGIH</td>
</tr>
<tr>
<td>Amiloride</td>
<td>17440-83-4</td>
<td>TWA</td>
<td>100 µg/m³</td>
<td>Internal</td>
</tr>
</tbody>
</table>

Engineering measures:
- Use feasible engineering controls to minimize exposure to compound.
- All engineering controls should be implemented by facility design and operated in accordance with GMP principles to protect products, workers, and the environment.

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:
-
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.

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.

SECTION 9. PHYSICAL AND CHEMICAL PROPERTIES

Appearance : powder
Color : pale red-brown
Odor : odorless
Odor 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 : No data available
Evaporation rate : No data available
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
Vapor pressure : No data available
Relative vapor density : No data available
Relative density : No data available
Density : No data available
Solubility(ies) : No data available
  Water solubility : No data available
Partition coefficient: n-octanol/water : No data available
Autoignition temperature : No data available
Decomposition temperature : No data available
Viscosity : Not explosive
  Viscosity, dynamic : No data available
  Viscosity, kinematic : No data available
Explosive properties : Not explosive
Oxidizing properties : The substance or mixture is not classified as oxidizing.
Molecular weight : 302.10 g/mol
Particle size : No data available

SECTION 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.

SECTION 11. TOXICOLOGICAL INFORMATION

Information on likely routes of exposure : Inhalation
  Skin contact
  Ingestion
  Eye contact

Acute toxicity
Harmful if swallowed.

Product:
Acute oral toxicity : Acute toxicity estimate: 1.785 mg/kg
  Method: Calculation method
Components:

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

Starch:
Acute oral toxicity : LD50 (Rat): > 5.000 mg/kg
Acute dermal toxicity : LD50 (Rabbit): > 2.000 mg/kg

Amiloride:
Acute oral toxicity : LD50 (Mouse): 56 mg/kg
LD50 (Rat): > 150 mg/kg

Skin corrosion/irritation
Not classified based on available information.

Components:

Hydrochlorothiazide:
Species : Rabbit
Result : No skin irritation

Amiloride:
Species : Rabbit
Result : Mild skin irritation
Remarks : slight irritation

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

Components:

Hydrochlorothiazide:
Species : Rabbit
Result : Mild eye irritation

Starch:
Species : Rabbit
Result : No eye irritation
Amiloride:  
Species: Rabbit  
Remarks: Severe eye irritation

Respiratory or skin sensitization  
Skin sensitization  
Not classified based on available information.  
Respiratory sensitization  
Not classified based on available information.

Components:

Starch:  
Test Type: Maximization Test  
Routes of exposure: Skin contact  
Species: Guinea pig  
Result: negative

Germ cell mutagenicity  
Not classified based on available information.

Components:

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 test  
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.
SAFETY DATA SHEET

Amiloride / Hydrochlorothiazide Formulation

Version 5.1  Revision Date: 01.10.2020  SDS Number: 44137-00014  Date of last issue: 23.03.2020  Date of first issue: 05.01.2015

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

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

Carcinogenicity
Not classified based on available information.

Components:

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

Amiloride:
Species : Rat
Application Route : Oral
Exposure time : 92 weeks
Result : negative

Species : Mouse
Application Route : Oral
Exposure time : 104 weeks
Result : negative

Reproductive toxicity
Not classified based on available information.

Components:

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 fetal 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.

Amiloride:  
Effects on fetal development  
: Test Type: Embryo-fetal development  
Species: Rabbit  
Application Route: Oral  
Result: No effects on fertility and early embryonic development were detected.

Test Type: Embryo-fetal development  
Species: Mouse  
Application Route: Oral  
Result: No effects on fertility and early embryonic development were detected.

STOT-single exposure  
Not classified based on available information.

STOT-repeated exposure  
Causes 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:  
Hydrochlorothiazide:  
Species  
: Rat, male and female  
LOAEL  
: 10 mg/kg  
Application Route  
: Oral  
Exposure time  
: 2 y
Target Organs: Kidney, Parathyroid gland
Species: Mouse, male and female
NOAEL: 300 - 550 mg/kg
Application Route: Oral
Exposure time: 2 y
Remarks: No significant adverse effects were reported

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

Starch:
Species: Rat
NOAEL: >= 2.000 mg/kg
Application Route: Skin contact
Exposure time: 28 Days
Method: OECD Test Guideline 410

Aspiration toxicity
Not classified based on available information.

Components:

Hydrochlorothiazide:
No aspiration toxicity classification

Experience with human exposure

Components:

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

Amiloride:
Ingestion: Symptoms: hyperkalemia

SECTION 12. ECOLOGICAL INFORMATION

Ecotoxicity

Components:

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
Amiloride:
Toxicity to daphnia and other aquatic invertebrates: EC50 (Daphnia magna (Water flea)): 56.3 mg/l
Exposure time: 48 h
Method: OECD Test Guideline 202

Persistence and degradability

Components:

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

SECTION 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.

SECTION 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.

SECTION 15. REGULATORY INFORMATION

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

Argentina. Carcinogenic Substances and Agents Registry: Not applicable
Control of precursors and essential chemicals for the preparation of drugs.

International Regulations

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

- **AICS**: not determined
- **DSL**: not determined
- **IECSC**: not determined

**SECTION 16. OTHER INFORMATION**

**Further information**

Sources of key data used to compile the Material Safety Data Sheet:


**Full text of other abbreviations**

- **ACGIH**: USA. ACGIH Threshold Limit Values (TLV)
- **AR OEL**: Argentina. Occupational Exposure Limits
- **ACGIH / TWA**: 8-hour, time-weighted average
- **AR OEL / CMP**: TLV (Threshold Limit Value)

AIIIC - Australian Inventory of Industrial Chemicals; ANTT - National Agency for Transport by Land of Brazil; ASTM - American Society for the Testing of Materials; bw - Body weight; CMR - Carcinogen, Mutagen or Reproductive Toxicant; DIN - Standard of the German Institute for Standardisation; DSL - Domestic Substances List (Canada); ECx - Concentration associated with x% response; ELx - Loading rate associated with x% response; EmS - Emergency Schedule; ENCS - Existing and New Chemical Substances (Japan); ErCx - Concentration associated with x% growth rate response; ERG - Emergency Response Guide; GHS - Globally Harmonized System; GLP - Good Laboratory Practice; IARC - International Agency for Research on Cancer; IATA - International Air Transport Association; IBC - International Code for the Construction and Equipment of Ships carrying Dangerous Chemicals in Bulk; IC50 - Half maximal inhibitory concentration; ICAO - International Civil Aviation Organization; IECSC - Inventory of Existing Chemical Substances in China; IMDG - International Maritime Dangerous Goods; IMO - International Maritime Organization; ISHL - Industrial Safety and Health Law (Japan); ISO - International Organisation for Standardization; KECI - Korea Existing Chemicals Inventory; LC50 - Lethal Concentration to 50% of a test population; LD50 - Lethal Dose to 50% of a test population (Median Lethal Dose); MARPOL - International Convention for the Prevention of Pollution from Ships; n.o.s. - Not Otherwise Specified; Nch - Chilean Norm; NO(A)EC - No Observed (Adverse) Effect Concentration; NO(A)EL - No Observed (Adverse) Effect Level; NOELR - No Observable Effect Loading Rate; NOM - Official Mexican Norm; NTP - National Toxicology Program; NZIoC - New Zealand Inventory of Chemicals; OECD - Organization for Economic Co-operation and Development; OPPTS - Office of Chemical Safety and Pollution Prevention; PBT - Persistent, Bioaccumulative and Toxic substance; PICCS - Philippines Inventory of Chemicals and Chemical Substances; (Q)SAR - (Quantitative) Structure Activity Relationship; REACH - Regulation (EC) No 1907/2006 of the European Parliament and of the Council concerning the Registration, Evaluation, Authorisation and Restriction of Chemicals; SADT - Self-Accelerating Decomposition Tempera-
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.