SAFETY DATA SHEET

Amiloride / Hydrochlorothiazide Formulation

Version: 5.0  Revision Date: 23.03.2020  SDS Number: 44151-00014  Date of last issue: 13.09.2019
Date of first issue: 05.01.2015

1. PRODUCT AND COMPANY IDENTIFICATION

   Product name: Amiloride / Hydrochlorothiazide Formulation

   Manufacturer or supplier’s details
   Company: MSD
   Address: Briahnager - Off Pune Nagar Road
            Wagholi - Pune - India  412 207
   Telephone: 908-740-4000
   Emergency telephone number: 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

2. HAZARDS IDENTIFICATION

Manufacture, Storage and Import of Hazardous Chemicals Rules 1989

Classification
Not classified as hazardous according to criteria laid down in Part I of Schedule-1.

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.
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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.

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>

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.
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
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 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: 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.
- 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.
- Take care to prevent spills, waste and minimize release to the environment.

Conditions for safe storage:
- Keep in properly labelled containers.
- 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>hydrochlorothiazide</td>
<td>58-93-5</td>
<td>TWA</td>
<td>100 µg/m³ (OEB 2)</td>
<td>Internal</td>
</tr>
<tr>
<td>Starch</td>
<td>9005-25-8</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.
Skin and body protection

Hygiene measures

Wear a faceshield or other full face protection if there is a potential for direct contact to the face with dusts, mists, or aerosols.

Work uniform or laboratory coat.

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

: pale red-brown

Odour

: odourless

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

: 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

Vapour pressure

: No data available

Relative vapour density

: No data available

Relative density

: No data available

Density

: No data available
Solubility(ies)
Water solubility : No data available
Partition coefficient: n-octanol/water : No data available
Auto-ignition temperature : No data available
Decomposition temperature : No data available
Viscosity
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

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
Harmful if swallowed.

Product:
Acute oral toxicity : Acute toxicity estimate: 1,785 mg/kg
Method: Calculation method

Components:
hydrochlorothiazide:
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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 sensitisation

Skin sensitisation
Not classified based on available information.

Respiratory sensitisation
Not classified based on available information.

Components:

Starch:
- Test Type: Maximisation Test
- Exposure routes: 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 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.

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: 10 mg/kg bw/day  
Result: negative

Species: Mouse  
Application Route: Oral  
Exposure time: 104 weeks: 8 mg/kg bw/day  
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 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

Amiloride:

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

Test Type: Embryo-foetal 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 yr  
Target Organs : Kidney, Parathyroid gland  
Species : Mouse, male and female  
NOAEL : 300 - 550 mg/kg
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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

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

Amiloride:
Ingestion : Symptoms: hyperkalemia

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 : EC50 (Daphnia magna (Water flea)): 56.3 mg/l
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12 aquatic invertebrates
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

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 IMO instruments
Not applicable for product as supplied.

15. REGULATORY INFORMATION

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

The components of this product are reported in the following inventories:
AICS: not determined
DSL: not determined
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IECSC : not determined

16. OTHER INFORMATION

Further information

Items where changes have been made to the previous version are highlighted in the body of this document by two vertical lines.

Date format : dd.mm.yyyy

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 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.

IN / EN