SAFETY DATA SHEET
Amiloride / Hydrochlorothiazide Formulation

SECTION 1. IDENTIFICATION

Product name : Amiloride / Hydrochlorothiazide Formulation
Other means of identification : No data available

Manufacturer or supplier’s details
Company name of supplier : Merck & Co., Inc
Address : 126 E. Lincoln Avenue
Rahway, New Jersey U.S.A. 07065
Telephone : 908-740-4000
Emergency telephone : 1-908-423-6000
E-mail address : EHSDATASTEWARD@merck.com

Recommended use of the chemical and restrictions on use
Recommended use : Pharmaceutical
Restrictions on use : Not applicable

SECTION 2. HAZARDS IDENTIFICATION

GHS classification in accordance with the Hazardous Products Regulations
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 doctor if you feel unwell. Rinse mouth.
P314 Get medical attention if you feel unwell.

Disposal:
P501 Dispose of contents and container to an approved waste disposal plant.
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Other hazards
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

<table>
<thead>
<tr>
<th>Substance / Mixture</th>
<th>Components</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hydrochlorothiazide</td>
<td>No data available</td>
</tr>
<tr>
<td>Starch</td>
<td>Sago starch</td>
</tr>
<tr>
<td>Amiloride</td>
<td>No data available</td>
</tr>
</tbody>
</table>

* Actual concentration or concentration range is withheld as a trade secret

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: Contact with dust can cause mechanical irritation or drying of the skin.
Dust contact with the eyes can lead to mechanical irritation.
Harmful if swallowed.
Causes damage to organs through prolonged or repeated exposure.

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
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 Self-reactive substances and mixtures 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 (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>CA AB OEL</td>
</tr>
<tr>
<td></td>
<td></td>
<td>TWA (Total dust)</td>
<td>10 mg/m³</td>
<td>CA BC OEL</td>
</tr>
<tr>
<td></td>
<td></td>
<td>TWA (respirable dust fraction)</td>
<td>3 mg/m³</td>
<td>CA BC OEL</td>
</tr>
<tr>
<td></td>
<td></td>
<td>TWAEV (total dust)</td>
<td>10 mg/m³</td>
<td>CA QC OEL</td>
</tr>
<tr>
<td>Amiloride</td>
<td>17440-83-4</td>
<td>TWA</td>
<td>100 µg/m³</td>
<td>ACGIH</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
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: No data available
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flammability limit
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)
Water solubility : No data available
Partition coefficient: n-octanol/water : No data available
Autoignition 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

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
- **Result:** negative
- **Test Type:** Bacterial reverse mutation assay (AMES)

### Starch:
- **Result:** negative
- **Test Type:** Bacterial reverse mutation assay (AMES)

### Amiloride:
- **Result:** negative
- **Test Type:** Bacterial reverse mutation assay (AMES)

### 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  
  **Exposure dose:** 10 mg/kg bw/day

- **Species:** Mouse
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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
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,
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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.
Do not dispose of waste into sewer.

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
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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.

Domestic regulation

TDG
Not regulated as a dangerous good

Special precautions for user
Not applicable

SECTION 15. REGULATORY INFORMATION

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

SECTION 16. OTHER INFORMATION

Full text of other abbreviations
ACGIH : USA. ACGIH Threshold Limit Values (TLV)
CA AB OEL : Canada. Alberta, Occupational Health and Safety Code (table 2; OEL)
CA BC OEL : Canada. British Columbia OEL
CA QC OEL : Québec. Regulation respecting occupational health and safety, Schedule 1, Part 1: Permissible exposure values for airborne contaminants
ACGIH / TWA : 8-hour, time-weighted average
CA AB OEL / TWA : 8-hour Occupational exposure limit
CA BC OEL / TWA : 8-hour time weighted average
CA QC OEL / TWAEV : Time-weighted average exposure value

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

Revision Date: 04/04/2023
Date format: mm/dd/yyyy

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

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.

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