SECTION 1. IDENTIFICATION

Product name: Amiloride / Hydrochlorothiazide Formulation

Manufacturer or supplier’s details
Company name of supplier: Merck & Co., Inc
Address: 2000 Galloping Hill Road
Kenilworth - New Jersey - U.S.A. 07033
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

SECTION 2. HAZARDS IDENTIFICATION

GHS classification in accordance with the OSHA Hazard Communication Standard (29 CFR 1910.1200)
Combustible dust

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:
- If small particles are generated during further processing, handling or by other means, may form combustible dust concentrations in air.
- 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.

Other hazards
Dust contact with the eyes can lead to mechanical irritation.
Contact with dust can cause mechanical irritation or drying of the skin.

SECTION 3. COMPOSITION/INFORMATION ON INGREDIENTS

Substance / Mixture: Mixture

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

Actual concentration 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: 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
Carbon dioxide (CO2)
Dry chemical

Unsuitable extinguishing media: None known.
media
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 spills 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.
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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 (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></td>
<td></td>
<td>TWA (Respirable)</td>
<td>5 mg/m³</td>
<td>NIOSH REL</td>
</tr>
<tr>
<td></td>
<td></td>
<td>TWA (total)</td>
<td>10 mg/m³</td>
<td>NIOSH REL</td>
</tr>
<tr>
<td></td>
<td></td>
<td>TWA (total dust)</td>
<td>15 mg/m³</td>
<td>OSHA Z-1</td>
</tr>
<tr>
<td></td>
<td></td>
<td>TWA (respirable fraction)</td>
<td>5 mg/m³</td>
<td>OSHA Z-1</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: General and local exhaust ventilation is recommended to maintain vapor exposures below recommended limits. Where concentrations are above recommended limits or are unknown, appropriate respiratory protection should be worn.
Follow OSHA respirator regulations (29 CFR 1910.134) and use NIOSH/MSHA approved respirators. Protection provided by air purifying respirators against exposure to any hazardous chemical is limited. Use a positive pressure air supplied respirator if there is any potential for uncontrolled release, exposure levels are unknown, or any other circumstance where air purifying respirators may not provide adequate protection.

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)
  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.

Incompatible materials
  Avoid dust formation.
  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
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
  - Result: negative

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

IARC
Group 2B: Possibly carcinogenic to humans
Hydrochlorothiazide 58-93-5

OSHA
No component of this product present at levels greater than or equal to 0.1% is on OSHA’s list of regulated carcinogens.

NTP
No ingredient of this product present at levels greater than or equal to 0.1% is identified as a known or anticipated carcinogen by NTP.

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, 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.
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.

Domestic regulation

49 CFR
Not regulated as a dangerous good

SECTION 15. REGULATORY INFORMATION

CERCLA Reportable Quantity
This material does not contain any components with a CERCLA RQ.

SARA 304 Extremely Hazardous Substances Reportable Quantity
This material does not contain any components with a section 304 EHS RQ.

SARA 302 Extremely Hazardous Substances Threshold Planning Quantity
This material does not contain any components with a section 302 EHS TPQ.

SARA 311/312 Hazards
- Combustible dust
- Acute toxicity (any route of exposure)
- Specific target organ toxicity (single or repeated exposure)

SARA 313
This material does not contain any chemical components with known CAS numbers that exceed the threshold (De Minimis) reporting levels established by SARA Title III, Section 313.

US State Regulations

Pennsylvania Right To Know
- D-Glucose, 4-O-beta-D-galactopyranosyl-, monohydrate 64044-51-5
- Calcium hydrogenorthophosphate dihydrate 7789-77-7
- Hydrochlorothiazide 58-93-5
- Starch 9005-25-8
- Guar gum 9000-30-0

California Permissible Exposure Limits for Chemical Contaminants
- Starch 9005-25-8

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

AICS : not determined
SECTION 16. OTHER INFORMATION

Further information

NFPA 704:

HMIS® IV:

HMIS® ratings are based on a 0-4 rating scale, with 0 representing minimal hazards or risks, and 4 representing significant hazards or risks. The "*" represents a chronic hazard, while the "/" represents the absence of a chronic hazard.

Full text of other abbreviations

ACGIH : USA. ACGIH Threshold Limit Values (TLV)
NIOSH REL : USA. NIOSH Recommended Exposure Limits
OSHA Z-1 : USA. Occupational Exposure Limits (OSHA) - Table Z-1 Limits for Air Contaminants
ACGIH / TWA : 8-hour, time-weighted average
NIOSH REL / TWA : Time-weighted average concentration for up to a 10-hour workday during a 40-hour workweek
OSHA Z-1 / TWA : 8-hour time weighted average

AIIC - Australian Inventory of Industrial Chemicals; ASTM - American Society for the Testing of Materials; bw - Body weight; CERCLA - Comprehensive Environmental Response, Compensation, and Liability Act; CMR - Carcinogen, Mutagen or Reproductive Toxicant; DIN - Standard of the German Institute for Standardisation; DOT - Department of Transportation; DSL - Domestic Substances List (Canada); ECx - Concentration associated with x% response; EHS - Extremely Hazardous Substance; 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; HMIS - Hazardous Materials Identification System; 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
SAFETY DATA SHEET

Amiloride / Hydrochlorothiazide Formulation

Version 7.1
Revision Date: 10/01/2020
SDS Number: 42692-00015
Date of last issue: 03/23/2020
Date of first issue: 01/05/2015

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

Revision Date: 10/01/2020

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.

US / Z8