

Amiloride / Hydrochlorothiazide Formulation

Version Revision Date: SDS Number: Date of last issue: 04/09/2022
6.6 10/01/2022 42677-00020 Date of first issue: 01/05/2015

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 : Category 1 (Kidney, Parathyroid gland)
- repeated exposure

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

Substance / Mixture : Mixture

Components

Chemical name	Common Name/Synonym	CAS-No.	Concentration (% w/w)
Hydrochlorothiazide	No data available	58-93-5	$\geq 10 - < 30$ *
Starch	Sago starch	9005-25-8	$\geq 10 - < 30$ *
Amiloride	No data available	17440-83-4	$\geq 1 - < 5$ *

* 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 : 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

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| | | Alcohol-resistant foam
Carbon dioxide (CO ₂)
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
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

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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

Components	CAS-No.	Value type (Form of exposure)	Control parameters / Permissible concentration	Basis
Hydrochlorothiazide	58-93-5	TWA	100 µg/m ³ (OEB 2)	Internal
Starch	9005-25-8	TWA	10 mg/m ³	CA AB OEL
		TWA (Total dust)	10 mg/m ³	CA BC OEL
		TWA (respirable dust fraction)	3 mg/m ³	CA BC OEL
		TWAEV (total dust)	10 mg/m ³	CA QC OEL
		TWA	10 mg/m ³	ACGIH
Amiloride	17440-83-4	TWA	100 µg/m ³	Internal

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
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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 | : | 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.

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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 : LD50 (Rat): 990 mg/kg
administration) 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

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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

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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

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Species : Rat
Application Route : Oral
Exposure time : 92 weeks
: 10 mg/kg bw/day
Result : negative

Species : Mouse

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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 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.

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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
 : 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,

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eye pain

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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 : EC50 (Daphnia magna (Water flea)): > 500 mg/l
aquatic invertebrates Exposure time: 48 h

Amiloride:

Toxicity to daphnia and other : EC50 (Daphnia magna (Water flea)): 56.3 mg/l
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

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

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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; TECI - Thailand Existing Chemicals Inventory; 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

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

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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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