

Amiloride / Hydrochlorothiazide Formulation

Version	Revision Date:	SDS Number:	Date of last issue: 09.04.2022
5.4	01.10.2022	42688-00018	Date of first issue: 05.01.2015

SECTION 1. PRODUCT AND COMPANY IDENTIFICATION

Product name : Amiloride / Hydrochlorothiazide Formulation

Manufacturer or supplier's details

Company name of supplier : MSD
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@msd.com

Recommended use of the chemical and restrictions on use

Recommended use : Pharmaceutical

Restrictions on use : Not applicable

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 or doctor/ physician 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 dis-
posal 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	CAS-No.	Concentration (% w/w)
Hydrochlorothiazide	58-93-5	≥ 20 -< 30
Starch	9005-25-8	≥ 10 -< 20
Amiloride	17440-83-4	≥ 1 -< 5

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.

Specific hazards during fire : Avoid generating dust; fine dust dispersed in air in sufficient

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fighting		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

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.

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- 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.
- 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.
- 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	VLE-PPT	10 mg/m ³	NOM-010-STPS-2014
		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 protect products, workers, and the environment.

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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.

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

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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
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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

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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
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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
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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.
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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.

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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.

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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

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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 : $\geq 2,000$ 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

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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.

Domestic regulation**NOM-002-SCT**

Not regulated as a dangerous good

Special precautions for user

Not applicable

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SECTION 15. REGULATORY INFORMATION**Safety, health and environmental regulations/legislation specific for the substance or mixture**

Federal Law for the control of chemical precursors, : Not applicable
essential chemical products and machinery for
producing capsules, tablets and pills.

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)
NOM-010-STPS-2014	: Mexico. Norm NOM-010-STPS-2014 on Chemicals Polluting the Work Environment - Identification, Assessment and Control - Appendix 1 Occupational Exposure Limits
ACGIH / TWA	: 8-hour, time-weighted average
NOM-010-STPS-2014 / VLE-	: Time weighted average limit value
PPT	

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 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-

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ture; 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 is considered as correct, but not exhaustive, and will be used only as a guide, which is based in the current knowledge of the substance or mixture, and is applicable to proper safety precautions for the product.

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