

Eplerenone

sc-203943

Material Safety Data Sheet



The Power is Question

Hazard Alert Code Key:

EXTREME

HIGH

MODERATE

LOW

Section 1 - CHEMICAL PRODUCT AND COMPANY IDENTIFICATION

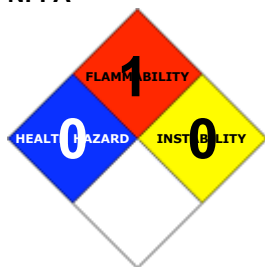
PRODUCT NAME

Eplerenone

STATEMENT OF HAZARDOUS NATURE

CONSIDERED A HAZARDOUS SUBSTANCE ACCORDING TO OSHA 29 CFR 1910.1200.

NFPA



SUPPLIER

Santa Cruz Biotechnology, Inc.
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EMERGENCY:

ChemWatch
Within the US & Canada: 877-715-9305
Outside the US & Canada: +800 2436 2255
(1-800-CHEMCALL) or call +613 9573 3112

SYNONYMS

C24-H30-O6, "7alpha, 11alpha, 17alpha)-9, 11-epoxy-17-hydroxy-3-oxopregn-4-ene-7, ", "21-dicarboxylic acid g-lactone methyl ester", "9alpha, 11-epoxy-7alpha-(methoxycarbonyl)-3-oxo-17alpha-pregn-4-ene-", "21, 17-carbolactone", "9alpha, 11alpha-epoxy-7alpha-methoxycarbonyl-20-spiro-4-ene-3, 21-", dione, "pregn-4-ene-7, 21-dicarboxylic acid, 9, 11-epoxy-17-hydroxy-3-oxo, ", "gamma-lactone, methyl ester (7alpha, 11alpha, 17alpha)", epoxymexrenone, CGP-30083, SC-66110, Inspra, "selective aldosterone receptor antagonist (SARA)", antihypertensive

Section 2 - HAZARDS IDENTIFICATION

CHEMWATCH HAZARD RATINGS

	Min	Max	
Flammability:	1		
Toxicity:	2		
Body Contact:	0		Min/Nil=0
Reactivity:	1		Low=1
Chronic:	2		Moderate=2
			High=3
			Extreme=4

CANADIAN WHMIS SYMBOLS

None

EMERGENCY OVERVIEW

RISK

POTENTIAL HEALTH EFFECTS

ACUTE HEALTH EFFECTS

SWALLOWED

- Accidental ingestion of the material may be damaging to the health of the individual.
- Gynaecomastia (enlarged breasts) may occur in males undertaking therapy
Spironolactone which has relatively slow onset of action with 2-3 days elapsing before maximum effect is produced (spironolactone also has a similarly slow diminishment of effect over 2 or 3 days on discontinuation).
Ingestion may give rise to headache, drowsiness and gastrointestinal disturbances, including cramp and diarrhoea. Other reported side-effects include ataxia, mental confusion, hirsutism, deepening of the voice, menstrual irregularities, impotence and skin rashes, enlargement of the breasts (gynaecomastia), which may persist, transient increases in blood urea-nitrogen, hyponatraemia and hypokalaemia.

EYE

- Although the material is not thought to be an irritant, direct contact with the eye may cause transient discomfort characterized by tearing or conjunctival redness (as with windburn). Slight abrasive damage may also result.

SKIN

- The material is not thought to produce adverse health effects or skin irritation following contact (as classified using animal models). Nevertheless, good hygiene practice requires that exposure be kept to a minimum and that suitable gloves be used in an occupational setting.
- Open cuts, abraded or irritated skin should not be exposed to this material.
- Entry into the blood-stream, through, for example, cuts, abrasions or lesions, may produce systemic injury with harmful effects. Examine the skin prior to the use of the material and ensure that any external damage is suitably protected.

INHALED

- The material is not thought to produce either adverse health effects or irritation of the respiratory tract following inhalation (as classified using animal models). Nevertheless, adverse effects have been produced following exposure of animals by at least one other route and good hygiene practice requires that exposure be kept to a minimum and that suitable control measures be used in an occupational setting.
- Persons with impaired respiratory function, airway diseases and conditions such as emphysema or chronic bronchitis, may incur further disability if excessive concentrations of particulate are inhaled.

CHRONIC HEALTH EFFECTS

- Exposure to the material may cause concerns for human fertility, on the basis that similar materials provide some evidence of impaired fertility in the absence of toxic effects, or evidence of impaired fertility occurring at around the same dose levels as other toxic effects, but which are not a secondary non-specific consequence of other toxic effects.

Exposure to the material may cause concerns for humans owing to possible developmental toxic effects, on the basis that similar materials tested in appropriate animal studies provide some suspicion of developmental toxicity in the absence of signs of marked maternal toxicity, or at around the same dose levels as other toxic effects but which are not a secondary non-specific consequence of other toxic effects.
Spironolactone produces thyroid and testicular tumours in rats. Potassium canrenoate, a metabolite of spironolactone in humans, caused resorption in the offspring of mice administered 80 mg/kg during 7-13 days of pregnancy.
Spironolactone was found to block testosterone secretion and increase progesterone concentration without inducing cell mortality in a primary culture of immature pig Leydig cells.
Long term exposure to high dust concentrations may cause changes in lung function i.e. pneumoconiosis; caused by particles less than 0.5 micron penetrating and remaining in the lung.

Section 3 - COMPOSITION / INFORMATION ON INGREDIENTS

NAME	CAS RN	%
eplerenone	107724-20-9	>98

Section 4 - FIRST AID MEASURES

SWALLOWED

· If swallowed do NOT induce vomiting. · If vomiting occurs, lean patient forward or place on left side (head-down position, if possible) to maintain open airway and prevent aspiration.

EYE

■ If this product comes in contact with the eyes: · Wash out immediately with fresh running water. · Ensure complete irrigation of the eye by keeping eyelids apart and away from eye and moving the eyelids by occasionally lifting the upper and lower lids.

SKIN

■ If skin or hair contact occurs: · Flush skin and hair with running water (and soap if available). · Seek medical attention in event of irritation.

INHALED

· If fumes or combustion products are inhaled remove from contaminated area. · Other measures are usually unnecessary.

NOTES TO PHYSICIAN

- For spironolactone intoxication:

Hyperkalaemia may be treated by giving a diuretic which causes excretion of potassium, by injection of dextrose with insulin or by the use of the appropriate ion-exchange resin.

Treat symptomatically.

No cases of human overdosage with eplerenone have been reported. Lethality was not observed in mice, rats, or dogs after single oral doses that provided C_{max} exposures at least 25 times higher than in humans receiving eplerenone 100 mg/day. Dogs showed emesis, salivation, and tremors at a C_{max} 41 times the human therapeutic C_{max}, progressing to sedation and convulsions at higher exposures.

The most likely manifestation of human overdosage would be anticipated to be hypotension or hyperkalemia. Eplerenone cannot be removed by hemodialysis. Eplerenone has been shown to bind extensively to charcoal. If symptomatic hypotension should occur, supportive treatment should be instituted. If hyperkalemia develops, standard treatment should be initiated.

Section 5 - FIRE FIGHTING MEASURES

Vapour Pressure (mmHG):	Negligible
Upper Explosive Limit (%):	Not Available
Specific Gravity (water=1):	Not Available
Lower Explosive Limit (%):	Not Available

EXTINGUISHING MEDIA

- Foam.
- Dry chemical powder.

FIRE FIGHTING

- Alert Emergency Responders and tell them location and nature of hazard.
- Wear breathing apparatus plus protective gloves.

GENERAL FIRE HAZARDS/HAZARDOUS COMBUSTIBLE PRODUCTS

- Combustible solid which burns but propagates flame with difficulty.
 - Avoid generating dust, particularly clouds of dust in a confined or unventilated space as dusts may form an explosive mixture with air, and any source of ignition, i.e. flame or spark, will cause fire or explosion. Dust clouds generated by the fine grinding of the solid are a particular hazard; accumulations of fine dust may burn rapidly and fiercely if ignited.
- Combustion products include: carbon monoxide (CO), carbon dioxide (CO₂), other pyrolysis products typical of burning organic material. May emit poisonous fumes.

FIRE INCOMPATIBILITY

- Avoid contamination with oxidizing agents i.e. nitrates, oxidizing acids, chlorine bleaches, pool chlorine etc. as ignition may result.

PERSONAL PROTECTION

Glasses:
Chemical goggles.
Gloves:
Respirator:
Particulate

Section 6 - ACCIDENTAL RELEASE MEASURES

MINOR SPILLS

- Clean up waste regularly and abnormal spills immediately.
- Avoid breathing dust and contact with skin and eyes.
- Wear protective clothing, gloves, safety glasses and dust respirator.
- Use dry clean up procedures and avoid generating dust.
- Vacuum up or sweep up. NOTE: Vacuum cleaner must be fitted with an exhaust micro filter (HEPA type) (consider explosion-proof machines designed to be grounded during storage and use).
- Dampen with water to prevent dusting before sweeping.
- Place in suitable containers for disposal.

MAJOR SPILLS

- Moderate hazard.
- CAUTION: Advise personnel in area.
- Alert Emergency Responders and tell them location and nature of hazard.

Section 7 - HANDLING AND STORAGE

PROCEDURE FOR HANDLING

- Avoid all personal contact, including inhalation.
 - Wear protective clothing when risk of exposure occurs.
- Empty containers may contain residual dust which has the potential to accumulate following settling. Such dusts may explode in the presence of an appropriate ignition source.
- Do NOT cut, drill, grind or weld such containers.
 - In addition ensure such activity is not performed near full, partially empty or empty containers without appropriate workplace safety authorisation or permit.

RECOMMENDED STORAGE METHODS

- Glass container.
- Polyethylene or polypropylene container.
- Check all containers are clearly labelled and free from leaks.

STORAGE REQUIREMENTS

- Store in original containers.
- Keep containers securely sealed.

Section 8 - EXPOSURE CONTROLS / PERSONAL PROTECTION

EXPOSURE CONTROLS

The following materials had no OELs on our records

- eplerenone: CAS:107724-20-9

PERSONAL PROTECTION



RESPIRATOR

Particulate

Consult your EHS staff for recommendations

EYE

- When handling very small quantities of the material eye protection may not be required.

For laboratory, larger scale or bulk handling or where regular exposure in an occupational setting occurs:

- Chemical goggles
- Face shield. Full face shield may be required for supplementary but never for primary protection of eyes
- Contact lenses may pose a special hazard; soft contact lenses may absorb and concentrate irritants. A written policy document, describing the wearing of lens or restrictions on use, should be created for each workplace or task. This should include a review of lens absorption and adsorption for the class of chemicals in use and an account of injury experience. Medical and first-aid personnel should be trained in their removal and suitable equipment should be readily available. In the event of chemical exposure, begin eye irrigation immediately and remove contact lens as soon as practicable. Lens should be removed at the first signs of eye redness or irritation - lens should be removed in a clean environment only after workers have washed hands thoroughly. [CDC NIOSH Current Intelligence Bulletin 59].

HANDS/FEET

- Suitability and durability of glove type is dependent on usage. Important factors in the selection of gloves include: such as:

- frequency and duration of contact,
- chemical resistance of glove material,
- glove thickness and
- dexterity

Select gloves tested to a relevant standard (e.g. Europe EN 374, US F739).

- When prolonged or frequently repeated contact may occur, a glove with a protection class of 5 or higher (breakthrough time greater than 240 minutes according to EN 374) is recommended.
- When only brief contact is expected, a glove with a protection class of 3 or higher (breakthrough time greater than 60 minutes according to EN 374) is recommended.
- Contaminated gloves should be replaced.

Gloves must only be worn on clean hands. After using gloves, hands should be washed and dried thoroughly. Application of a non-perfumed moisturiser is recommended.

- Rubber gloves (nitrile or low-protein, powder-free latex). Employees allergic to latex gloves should use nitrile gloves in preference.
- Double gloving should be considered.
- PVC gloves.
- Protective shoe covers.
- Head covering.

Experience indicates that the following polymers are suitable as glove materials for protection against undissolved, dry solids, where abrasive particles are not present.

- polychloroprene
- nitrile rubber
- butyl rubber
- fluorocautchouc
- polyvinyl chloride

Gloves should be examined for wear and/ or degradation constantly.

OTHER

- For quantities up to 500 grams a laboratory coat may be suitable.
- For quantities up to 1 kilogram a disposable laboratory coat or coverall of low permeability is recommended. Coveralls should be buttoned at collar and cuffs.
- For quantities over 1 kilogram and manufacturing operations, wear disposable coverall of low permeability and disposable shoe covers.
- For manufacturing operations, air-supplied full body suits may be required for the provision of advanced respiratory protection.

- Eye wash unit.
- Ensure there is ready access to an emergency shower.
- For Emergencies: Vinyl suit.

ENGINEERING CONTROLS

- Enclosed local exhaust ventilation is required at points of dust, fume or vapor generation.
- HEPA terminated local exhaust ventilation should be considered at point of generation of dust, fumes or vapors.

Section 9 - PHYSICAL AND CHEMICAL PROPERTIES

PHYSICAL PROPERTIES

State	Divided Solid	Molecular Weight	414.49
Melting Range (°F)	464- 467.6	Viscosity	Not Applicable
Boiling Range (°F)	Not Applicable	Solubility in water (g/L)	Partly Miscible
Flash Point (°F)	Not Available	pH (1% solution)	Not Applicable
Decomposition Temp (°F)	Not Available	pH (as supplied)	Not Applicable
Autoignition Temp (°F)	Not Available	Vapour Pressure (mmHG)	Negligible
Upper Explosive Limit (%)	Not Available	Specific Gravity (water=1)	Not Available
Lower Explosive Limit (%)	Not Available	Relative Vapor Density (air=1)	Not Applicable
Volatile Component (%vol)	Negligible	Evaporation Rate	Not Applicable

APPEARANCE

Crystalline solid; does not mix well with water. Soluble in dichloromethane, acetonitrile; slightly soluble in ethanol; sparingly soluble in methyl ethyl ketone, methanol; very slightly soluble in water.

Section 10 - CHEMICAL STABILITY

CONDITIONS CONTRIBUTING TO INSTABILITY

- Presence of incompatible materials.
- Product is considered stable.

STORAGE INCOMPATIBILITY

- Avoid reaction with oxidizing agents.

For incompatible materials - refer to Section 7 - Handling and Storage.

Section 11 - TOXICOLOGICAL INFORMATION

EPLERENONE

TOXICITY AND IRRITATION

EPLERENONE:

- No significant acute toxicological data identified in literature search.

Carcinogenesis, Mutagenesis, Impairment of Fertility

Eplerenone was non-genotoxic in a battery of assays including in vitro bacterial mutagenesis (Ames test in Salmonella spp. and E. Coli), in vitro mammalian cell mutagenesis (mouse lymphoma cells), in vitro chromosomal aberration (Chinese hamster ovary cells), in vivo rat bone marrow micronucleus formation, and in vivo/ex vivo unscheduled DNA synthesis in rat liver.

There was no drug-related tumor response in heterozygous P53 deficient mice when tested for 6 months at dosages up to 1000 mg/kg/day (systemic AUC exposures up to 9 times the exposure in humans receiving the 100 mg/day therapeutic dose). Statistically significant increases in benign thyroid tumors were observed after 2 years in both male and female rats when administered eplerenone 250 mg/kg/day (highest dose tested) and in male rats only at 75 mg/kg/day. These dosages provided systemic AUC exposures approximately 2 to 12 times higher than the average human therapeutic exposure at 100 mg/day. Repeat dose administration of eplerenone to rats increases the hepatic conjugation and clearance of thyroxine, which results in increased levels of TSH by a compensatory mechanism. Drugs that have produced thyroid tumors by this rodent- specific mechanism have not shown a similar effect in humans.

Male rats treated with eplerenone at 1000 mg/kg/day for 10 weeks (AUC 17 times that at the 100 mg/day human therapeutic dose) had decreased weights of seminal vesicles and epididymides and slightly decreased fertility. Dogs administered eplerenone at dosages of 15 mg/kg/day and higher (AUC 5 times that at the 100 mg/day human therapeutic dose) had dose-related prostate atrophy. The prostate atrophy was reversible after daily treatment for 1 year at 100 mg/kg/day. Dogs with prostate atrophy showed no decline in libido, sexual performance, or semen quality. Testicular weight and histology were not affected by eplerenone in any test animal species at any dosage.

Teratogenic Effects

Embryo-fetal development studies were conducted with doses up to 1000 mg/kg/day in rats and 300 mg/kg/day in rabbits (exposures up to 32 and 31 times the human AUC for the 100 mg/day therapeutic dose, respectively). No teratogenic effects were seen in rats or rabbits, although decreased body weight in maternal rabbits and increased rabbit fetal resorptions and post-implantation loss were observed at the highest administered dosage

Section 12 - ECOLOGICAL INFORMATION

No data

Section 13 - DISPOSAL CONSIDERATIONS

Disposal Instructions

All waste must be handled in accordance with local, state and federal regulations.

‡ Legislation addressing waste disposal requirements may differ by country, state and/ or territory. Each user must refer to laws operating in their area. In some areas, certain wastes must be tracked.

A Hierarchy of Controls seems to be common - the user should investigate:

- Reduction
- Reuse
- Recycling
- Disposal (if all else fails)

This material may be recycled if unused, or if it has not been contaminated so as to make it unsuitable for its intended use. Shelf life considerations should also be applied in making decisions of this type. Note that properties of a material may change in use, and recycling or reuse may not always be appropriate.

DO NOT allow wash water from cleaning equipment to enter drains. Collect all wash water for treatment before disposal.

- Recycle wherever possible.
- Consult manufacturer for recycling options or consult Waste Management Authority for disposal if no suitable treatment or disposal facility can be identified.

Section 14 - TRANSPORTATION INFORMATION

NOT REGULATED FOR TRANSPORT OF DANGEROUS GOODS: DOT, IATA, IMDG

Section 15 - REGULATORY INFORMATION

No data for eplerenone (CAS: , 107724-20-9)

Section 16 - OTHER INFORMATION

LIMITED EVIDENCE

- Ingestion may produce health damage*.
 - May possibly affect fertility*.
 - May possibly be harmful to the foetus/ embryo*.
- * (limited evidence).

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- Classification of the preparation and its individual components has drawn on official and authoritative sources as well as independent review by the Chemwatch Classification committee using available literature references.

A list of reference resources used to assist the committee may be found at:
www.chemwatch.net/references.

- The (M)SDS is a Hazard Communication tool and should be used to assist in the Risk Assessment. Many factors determine whether the reported Hazards are Risks in the workplace or other settings. Risks may be determined by reference to Exposures Scenarios. Scale of use, frequency of use and current or available engineering controls must be considered.

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