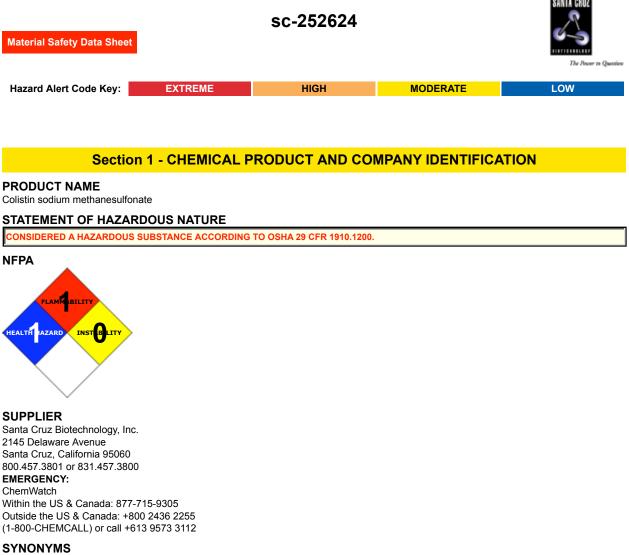
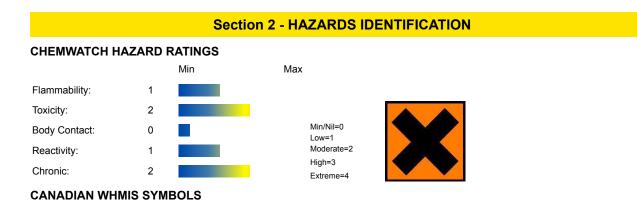
# Colistin sodium methanesulfonate



C58-H105-N16-Na5-O28-S5, "colistinmethanesulfonic acid, pentasodium salt", "colistin sulfomethate sodium", Alficetin, CLM, "Colimycin M", Colimycine, "colistimethate sodium", Colomycin, colistinat, "colistin sodium methanesulfonate", Coly-Mycin, "Colymycin M", "2, 5, 8, 11, 14, 17, 20-heptaoxo-4, 13, 16-tris[2-(sulfona", "tomethylamino)ethyl]-3, 6, 9, 12, 15, 18, 21-heptazacycl", otricos-1-yl]amino]-1-oxo-4-(sulfonatomethylamino), butan-2-yl]amino]-1-oxobutan-2-yl]amino]-3-(6-meth, yloctanoylamino)-4-oxobutyl]amino]methanesulfonate, "pentasodium colistinmethanesulfonate", "pentasodium [[4-[[3-hydroxy-1-[[1-[[19-(1-hydroxyethyl)-7, 10-bis(2-", methylpropyl)-, "sodium colistinemethanesulfonate", Methacolimycin, W-1929, antibiotic





## **EMERGENCY OVERVIEW**

RISK

Harmful if swallowed.

POTENTIAL HEALTH EFFECTS

## **ACUTE HEALTH EFFECTS**

## **SWALLOWED**

Accidental ingestion of the material may be harmful; animal experiments indicate that ingestion of less than 150 gram may be fatal or may produce serious damage to the health of the individual.

#### 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.

## <\p>.

## SKIN

Skin contact is not thought to produce harmful health effects (as classified using animal models). Systemic harm, however, has been identified following exposure of animals by at least one other route and the material may still produce health damage following entry through wounds, lesions or abrasions.

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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 respiratory irritation (as classified using animal models). Nevertheless inhalation of dusts, or fume, especially for prolonged periods, may produce respiratory discomfort and occasionally, distress.

Inhalation of dusts, generated by the material during the course of normal handling, may be damaging to the health of the individual.

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**

Limited evidence suggests that repeated or long-term occupational exposure may produce cumulative health effects involving organs or biochemical systems.

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.

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Prolonged or repeated use of antibiotics, at therapeutic doses, may produce bacterial resistance for some types of bacteria. Prolonged use may result in the overgrowth of non-susceptible organisms (i.e.

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Exposure to small quantities may induce hypersensitivity reactions characterized by acute bronchospasm, hives (urticaria), deep dermal wheals (angioneurotic edema), running nose (rhinitis) and blurred vision . Anaphylactic shock and skin rash (non-thrombocytopenic purpura) may occur. <\p>.

# Section 3 - COMPOSITION / INFORMATION ON INGREDIENTS

NAME	CAS RN	%
colistimethate sodium	8068-28-8	>98

# Section 4 - FIRST AID MEASURES

## **SWALLOWED**

· IF SWALLOWED, REFER FOR MEDICAL ATTENTION, WHERE POSSIBLE, WITHOUT DELAY. · Where Medical attention is not immediately available or where the patient is more than 15 minutes from a hospital or unless instructed otherwise:

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. · Lay patient down. Keep warm and rested.

■ for poisons (where specific treatment regime is absent):

-----BASIC TREATMENT

· Establish a patent airway with suction where necessary.

· Watch for signs of respiratory insufficiency and assist ventilation as necessary.

Treat symptomatically.

For colistin intoxication:

Overdosage with colistimethate sodium can cause neuromuscular blockade characterized by paresthesia, lethargy, confusion, dizziness, ataxia, nystagmus, disorders of speech and apnea. Respiratory muscle paralysis may lead to apnea, respiratory arrest and death. Overdosage with the drug can also cause acute renal failure, manifested as decreased urine output and increases in serum concentrations of BUN and creatinine.

It is unknown whether colistimethate sodium can be removed by hemodialysis or peritoneal dialysis in overdose cases.

# Section 5 - FIRE FIGHTING MEASURES

Vapour Pressure (mmHG):	Not applicable.
Upper Explosive Limit (%):	Not available
Specific Gravity (water=1):	Not available.
Lower Explosive Limit (%):	Not available

## **EXTINGUISHING MEDIA**

· Water spray or fog.

· Foam.

#### 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), nitrogen oxides (NOx), sulfur oxides (SOx), 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.
- $\cdot$  Keep containers securely sealed.

# Section 8 - EXPOSURE CONTROLS / PERSONAL PROTECTION

## **EXPOSURE CONTROLS**

The following materials had no OELs on our records • colistimethate sodium: CAS:8068-28-8 CAS:82497-00-5

## 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
- · fluorocaoutchouc

· 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

Solid. Mixes with water.			
State	Divided solid	Molecular Weight	1749.81
Melting Range (°F)	Not available	Viscosity	Not Applicable
Boiling Range (°F)	Not applicable	Solubility in water (g/L)	Miscible
Flash Point (°F)	Not available	pH (1% solution)	6.2-7.5
Decomposition Temp (°F)	Not Available	pH (as supplied)	Not applicable
Autoignition Temp (°F)	Not available	Vapour Pressure (mmHG)	Not applicable.
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)	Not applicable.	Evaporation Rate	Not applicable

## APPEARANCE

White, odourless, powder with bitter taste; mixes with water (1:<2).

## Section 10 - CHEMICAL STABILITY

## CONDITIONS CONTRIBUTING TO INSTABILITY

 $\cdot$  Presence of incompatible materials.

 $\cdot$  Product is considered stable.

## STORAGE INCOMPATIBILITY

· Avoid strong acids, bases. Avoid reaction with oxidizing agents.

wold redotion with oxidizing agents.

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

# Section 11 - TOXICOLOGICAL INFORMATION

**IRRITATION** 

## COLISTIMETHATE SODIUM

## TOXICITY AND IRRITATION

COLISTIMETHATE SODIUM: • unless otherwise specified data extracted from RTECS - Register of Toxic Effects of Chemical Substances.

TOV	ICITY
104	

Oral (rat) LD50: 5450 mg/kg

Intraperitoneal (rat) LD50: 86 mg/kg

Subcutaneous (rat) LD50: 87 mg/kg

Intramuscular (rat) LD50: 44 mg/kg

Oral (mouse) LD50: >766 mg/kg

Intraperitoneal (mouse) LD50: 126 mg/kg

Subcutaneous (mouse) LD50: 138 mg/kg

Intramuscular (mouse) LD50: 748 mg/kg

Intramuscular (rabbit) LD50: 465 mg/kg

The following adverse reactions have been reported with colistimethate sodium (syn: colistin sulfomethate

## sodium):

Gastrointestinal: gastrointestinal upset

Nervous System: tingling of extremities and tongue, slurred speech, dizziness, vertigo and paresthesia Integumentary: generalized itching, urticaria and rash

Body as a Whole: fever

Laboratory Deviations: increased blood urea nitrogen (BUN), elevated creatinine and decreased creatinine clearance

Respiratory System:respiratory distress and apnea

Renal System: nephrotoxicity and decreased urine output

Transient neurological disturbances may occur. These include circumoral paraesthesia or numbness, tingling or formication of the extremities, generalized pruritus, vertigo, dizziness, and slurring of speech. Reduction of dosage may alleviate symptoms. Therapy need not be discontinued, but such patients should be observed with particular care.

Respiratory arrest has been reported following intramuscular administration of colistimethate sodium. Impaired renal function increases the possibility of apnea and neuromuscular blockade following administration of colistimethate sodium

The main toxicities described with intravenous treatment are nephrotoxicity (damage to the kidneys) and neurotoxicity (damage to the nerves) but this may reflect the very high doses given, which are much higher than the doses currently recommended by any manufacturer and for which no adjustment was made for renal disease. Neuro- and nephrotoxic effects appear to be transient and subside on discontinuation of therapy or reduction in dose .

At a dose of 160 mg colistimethate IV every eight hours, very little nephrotoxicity is seen. Indeed, colistin appears to have less toxicity than the aminoglycosides that subsequently replaced it, and colistin has been used for extended periods of up to six months with no ill effects.

The main toxicity described with aerosolised treatment is bronchospasm which can be treated or prevented with the use of beta2-agonists such as salbutamol or following a desensitisation protocol

Long-term animal carcinogenicity studies and genetic toxicology studies have not been performed with colistimethate sodium. There were no adverse effects on fertility or reproduction in rats at doses of 9.3 mg/kg/day (0.30 times the maximum daily human dose when based on ma/m2).

Colistimethate sodium given intramuscularly during organogenesis to rabbits at 4.15 and 9.3 mg/kg resulted in talipes varus in 2.6% and 2.9% of foetuses, respectively. These doses are 0.25 and 0.55 times the maximum daily human dose based on mg/m2. In addition, increased resorption occurred at 9.3 mg/kg. Colistimethate sodium was not teratogenic in rats at 4.15 or 9.3 mg/kg. These doses are 0.13 and 0.30 times the maximum daily human dose based on mg/m2. Since colistimethate sodium is transferred across the placental barrier in humans, it should be used during pregnancy only if the potential benefit justifies the potential risk to the foetus.

Intramuscular (child) LDLo:90 mg/kg/18h-I

# 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.

Puncture containers to prevent re-use and bury at an authorized landfill.

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

colistimethate sodium (CAS: 8068-28-8.82497-00-5) is found on the following regulatory lists; "Canada Non-Domestic Substances List (NDSL)","US Toxic Substances Control Act (TSCA) - Inventory"

# Section 16 - OTHER INFORMATION

## LIMITED EVIDENCE

- Inhalation may produce health damage\*.
- Cumulative effects may result following exposure\*.
- \* (limited evidence).

## Ingredients with multiple CAS Nos

Ingredient Name CAS colistimethate sodium 8068-28-8, 82497-00-5

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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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