

Mivacurium Chloride

sc-204809



The Power is Question

Material Safety Data Sheet

Hazard Alert Code Key:

EXTREME

HIGH

MODERATE

LOW

Section 1 - CHEMICAL PRODUCT AND COMPANY IDENTIFICATION

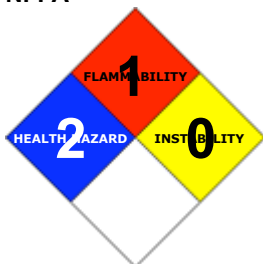
PRODUCT NAME

Mivacurium Chloride

STATEMENT OF HAZARDOUS NATURE

CONSIDERED A HAZARDOUS SUBSTANCE ACCORDING TO OSHA 29 CFR 1910.1200.

NFPA



SUPPLIER

Santa Cruz Biotechnology, Inc.
2145 Delaware Avenue
Santa Cruz, California 95060
800.457.3801 or 831.457.3800

EMERGENCY

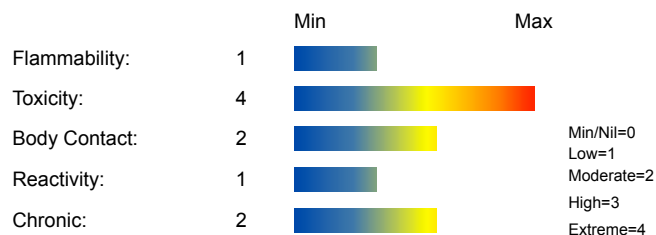
ChemWatch
Within the US & Canada: 877-715-9305
Outside the US & Canada: +800 2436 2255
(1-800-CHEMCALL) or call +613 9573 3112

SYNONYMS

C58-H80-Cl2-N2-O14, Mivacron, "BW B109OU dichloride", "bis[3-[6, 7-dimethoxy-2-methyl-1-[(3, 4, 5-trimethoxyphenyl)methyl]-3, ", "4-dihydro-1H-isoquinolin-2-yl] propyl] oct-4-enedioate dichloride", "bisbenzylisoquinolinium neuromuscular blocker/ muscle relaxant"

Section 2 - HAZARDS IDENTIFICATION

CHEMWATCH HAZARD RATINGS



CANADIAN WHMIS SYMBOLS



EMERGENCY OVERVIEW

RISK

POTENTIAL HEALTH EFFECTS

ACUTE HEALTH EFFECTS

SWALLOWED

■ Accidental ingestion of the material may be severely damaging to the health of the individual; animal experiments indicate that ingestion of less than 5 gram may be fatal.

■ Tubocurarine and its structural analogues rarely produces side-effects at levels employed during anaesthesia but in overdose may cause respiratory failure (by paralyzing intercostal muscles and the diaphragm) and hypotension.

Regurgitation of stomach contents may also occur as a result of relaxation of the oesophageal muscle and sphincters.

■ Drugs which activate nicotine receptors (one type of cholinergic receptor), primarily affect the neuromuscular junction, producing, for example, fasciculations, weakness and paralysis.

Activation of the receptor by cholinergic agonists initially stimulates autonomic ganglia and neuromuscular junctions, and then, in high doses, produces blockade.

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 be a skin irritant (as classified using animal models).

Abrasive damage however, may result from prolonged exposures.

■ Skin contact with the material may damage the health of the individual; systemic effects may result following absorption.

■ 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.

There is limited evidence that, skin contact with this product is more likely to cause a sensitization reaction in some persons compared to the general population.

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.

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.

The benzyloisoquinoline alkaloids (BIAs) are a complex and diverse group of natural products consisting of more than 2500 known structures. The general role of alkaloids in the chemical defense of plants against herbivores and pathogens suggests that BIAs contribute to the reproductive fitness of plants with the ability to produce these compounds.

Certain benzyloisoquinoline compounds used in neuromuscular blockade have a tendency to release histamine, particularly at higher doses.

Based on initial clinical practice experience in patients who received the drug, spontaneously reported adverse events are uncommon. Some of these events occurred at recommended doses and required treatment. There are insufficient data to establish a causal relationship or to support an estimate of their incidence. Adverse events reported during clinical practice include:

General: Allergic reactions which, in rare instances, were severe

Musculoskeletal: Diminished drug effect, prolonged drug effect

Cardiovascular: Hypotension (rarely severe), flushing

Respiratory: Bronchospasm

Integumentary: Rash

Section 3 - COMPOSITION / INFORMATION ON INGREDIENTS

NAME	CAS RN	%
mivacurium hydrochloride	106861-44-3	>98v

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: · Immediately hold eyelids apart and flush the eye continuously with 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 contact occurs: · Immediately remove all contaminated clothing, including footwear · Flush skin and hair with running water (and soap if available).

INHALED

· If fumes or combustion products are inhaled remove from contaminated area. · Lay patient down. Keep warm and rested.

NOTES TO PHYSICIAN

■ Treatment of overdose or intoxication by tubocurarine and its structural analogues:

- In respiratory failure, respiration should be assisted.
- Neostigmine methylsulfate should be given intravenously in a dose of 2 to 3 mg over 60 secs with 0.6 to 1.2 mg of atropine sulfate.
- Additional neostigmine may be given but a total dose of 5 mg should not be exceeded.

MARTINDALE: The Extra Pharmacopoeia, 29th Edition.

For neuromuscular blocking agents:

· Overdosage with neuromuscular blocking agents may result in neuromuscular block beyond the time needed for surgery and anesthesia. Neuromuscular blocking agents may have a profound effect in patients with neuromuscular diseases (e.g., myasthenia gravis and the myasthenic syndrome). In these and other conditions in which prolonged neuromuscular block is a possibility (e.g., carcinomatosis), ensure a peripheral nerve stimulator is available.

· The primary treatment is maintenance of a patent airway and controlled ventilation until recovery of normal neuromuscular function is assured.

· Once evidence of recovery from neuromuscular block is observed, further recovery may be facilitated by administration of an anticholinesterase agent (e.g., neostigmine, edrophonium) in conjunction with an appropriate anticholinergic agent (see Antagonism of Neuromuscular Block subsection below).

· Overdosage with neuromuscular blocking agents may result in neuromuscular block beyond the time needed for surgery and anesthesia. The primary treatment is maintenance of a patent airway and controlled ventilation until recovery of normal neuromuscular function is assured. Once recovery from neuromuscular block begins, further recovery may be facilitated by administration of an anticholinesterase agent (e.g., neostigmine, edrophonium) in conjunction with an appropriate anticholinergic agent such as atropine.

· The possibility of iatrogenic overdosage can be minimised by carefully monitoring muscle twitch response to peripheral nerve stimulation. Overdosage may increase the risk of histamine release and cardiovascular effects, especially hypotension. If cardiovascular support is necessary, this should include proper positioning, fluid administration, and the use of vasopressor agents if necessary. A longer duration of neuromuscular blockade may result from overdosage and a peripheral nerve stimulator should be used to monitor recovery.

· Antagonism of Neuromuscular Block: Antagonists (such as neostigmine and edrophonium) should not be administered when complete neuromuscular block is evident or suspected. The use of a peripheral nerve stimulator to evaluate recovery and antagonism of neuromuscular block is recommended.

· Patients administered antagonists should be evaluated for adequate clinical evidence of antagonism, e.g., 5-second head lift and grip strength. Ventilation must be supported until no longer required.

· Antagonism may be delayed in the presence of debilitation, carcinomatosis, and the concomitant use of certain broad spectrum antibiotics, or anesthetic agents and other drugs which enhance neuromuscular block or separately cause respiratory depression. Under such circumstances the management is the same as that of prolonged neuromuscular block.

· Patients with burns have been shown to develop resistance to nondepolarizing neuromuscular blocking agents, including atracurium. The extent of altered response depends upon the size of the burn and the time elapsed since the burn injury.

· Patients with hemiparesis or paraparesis also may demonstrate resistance to nondepolarizing muscle relaxants in the affected limbs. To avoid inaccurate dosing, neuromuscular monitoring should be performed on a non-paretic limb.

· Acid-base and/or serum electrolyte abnormalities may potentiate or antagonize the action of neuromuscular blocking agents.

The mean elimination half-life of mivacurium ranges from 1.7 to 2.6 minutes in healthy, young adults administered 0.1 to 0.25 mg/kg mivacurium. Mean plasma clearance rates range from 40 to 70 mL/min/kg and mean steady-state volume of distribution values range from 0.08 to 0.11 L/kg. The short elimination half-life and high clearance are consistent with the short duration of action of mivacurium

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

- Water spray or fog.
- Foam.

FIRE FIGHTING

- Alert Emergency Responders and tell them location and nature of hazard.
- Wear full body protective clothing with breathing apparatus.

When any large container (including road and rail tankers) is involved in a fire, consider evacuation by 800 metres in all directions.

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), hydrogen chloride, phosgene, nitrogen oxides (NO_x), 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:

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

- Clear area of personnel and move upwind.
- 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.

- Lined metal can, Lined metal pail/drum
- Plastic pail.

For low viscosity materials

- Drums and jerricans must be of the non-removable head type.
- Where a can is to be used as an inner package, the can must have a screwed enclosure.

STORAGE REQUIREMENTS

- Store in original containers.
- Keep containers securely sealed.
- Store at room temperature.

Section 8 - EXPOSURE CONTROLS / PERSONAL PROTECTION

EXPOSURE CONTROLS

The following materials had no OELs on our records

- mivacurium hydrochloride: CAS:106861-44-3

PERSONAL PROTECTION



RESPIRATOR

- particulate.

Consult your EHS staff for recommendations

EYE

- 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

■ NOTE: The material may produce skin sensitization in predisposed individuals. Care must be taken, when removing gloves and other protective equipment, to avoid all possible skin contact.

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.

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

Mixes with water.

State	Divided Solid	Molecular Weight	1100.17
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)	Not Available
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; mixes with water. Kow 0.015 Mivacurium chloride is a mixture of three stereoisomers: (1R, 1'R, 2S, 2'S), the trans-trans diester; (1R, 1'R, 2R, 2'S), the cis-trans diester; and (1R, 1'R, 2R, 2'R), the cis-cis diester. The trans-trans and cis-trans stereoisomers comprise 92% to 96% of mivacurium chloride and their neuromuscular blocking potencies are not significantly different from each other or from mivacurium chloride. The cis-cis diester has been estimated from studies in cats to have one tenth the neuromuscular blocking potency of the other two stereoisomers.

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

mivacurium hydrochloride

TOXICITY AND IRRITATION

MIVACURIUM HYDROCHLORIDE:

- unless otherwise specified data extracted from RTECS - Register of Toxic Effects of Chemical Substances.

■ Most neuromuscular blocking agents facilitate histamine release in susceptible patients. Adverse reactions include skin flushing, transient hypotension, hypertension, tachycardia, bradycardia, bronchospasm and anaphylactoid reactions.

Mivacurium hydrochloride was non-mutagenic in the Ames Salmonella assay, the mouse lymphoma assay, the human lymphocyte assay, and the in vivo rat bone marrow cytogenetic assay.

Teratology testing in nonventilated pregnant rats and mice treated subcutaneously with maximum subparalyzing doses of the drug revealed no maternal or fetal toxicity or teratogenic effects. There are no adequate and well-controlled studies of the drug in pregnant women. Because animal studies are not always predictive of human response, and the doses used were subparalyzing, the drug should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus.

MIVACRON (a mixture of three stereoisomers) was well tolerated during extensive clinical trials in inpatients and outpatients. Prolonged neuromuscular block, which is an important adverse experience associated with neuromuscular blocking agents as a class, was reported as an adverse experience in three of 2,074 patients administered MIVACRON. The most commonly reported adverse experience following the administration of MIVACRON was transient, dose-dependent cutaneous flushing about the face, neck, and/or chest. Flushing was most frequently noted after the initial dose of MIVACRON and was reported in about 25% of adult patients who received 0.15 mg/kg MIVACRON over 5 to 15 seconds. When present, flushing typically began within 1 to 2 minutes after the dose of MIVACRON and lasted for 3 to 5 minutes. Of 105 patients who experienced flushing after 0.15 mg/kg MIVACRON, two patients also experienced mild hypotension that was not treated, and one patient experienced moderate wheezing that was successfully treated.

Overall, hypotension was infrequently reported as an adverse experience in the clinical trials of MIVACRON. One of 332 (0.3%) healthy adults who received 0.15 mg/kg MIVACRON over 5 to 15 seconds and none of 37 cardiac surgery patients who received 0.15 mg/kg MIVACRON over 60 seconds were treated for a decrease in blood pressure in association with the administration of MIVACRON. One to two percent of healthy adults given 0.20 mg/kg MIVACRON over 5 to 15 seconds, 2% to 3% of healthy adults given 0.20 mg/kg over 30 seconds, none of 100 healthy adults given 0.25 mg/kg as a divided dose (0.15 mg/kg followed in 30 seconds by 0.10 mg/kg), and 2% to 4% of cardiac surgery patients given 0.20 mg/kg over 60 seconds were treated for a decrease in blood pressure. None of the 63 children who received the recommended dose of 0.20 mg/kg MIVACRON was treated for a decrease in blood pressure in association with the administration of MIVACRON.

Section 12 - ECOLOGICAL INFORMATION

This material and its container must be disposed of as hazardous waste.

Ecotoxicity

Ingredient	Persistence: Water/Soil	Persistence: Air	Bioaccumulation	Mobility
mivacurium hydrochloride	No Data Available	No Data Available		

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

DOT:

Symbols: None Hazard class or Division: 6.1

Identification Numbers: UN3249 PG: III

Label Codes: 6.1 Special provisions: T1, TP33
Packaging: Exceptions: 153 Packaging: Non- bulk: 213
Packaging: Exceptions: 153 Quantity limitations: 5 kg
Passenger aircraft/rail:
Quantity Limitations: Cargo 5 kg Vessel stowage: Location: C
aircraft only:
Vessel stowage: Other: 40
Hazardous materials descriptions and proper shipping names:
Medicine, solid, toxic, n.o.s.

Air Transport IATA:

UN/ID Number: 3249 Packing Group: III
Special provisions: A3
Cargo Only
Packing Instructions: 200 kg Maximum Qty/Pack: 677
Passenger and Cargo Passenger and Cargo
Packing Instructions: 100 kg Maximum Qty/Pack: 670
Passenger and Cargo Limited Quantity Passenger and Cargo Limited Quantity
Packing Instructions: 5 kg Maximum Qty/Pack: Y645
Shipping Name: MEDICINE, SOLID, TOXIC, N.O.S.(CONTAINS
MIVACURIUM HYDROCHLORIDE)

Maritime Transport IMDG:

IMDG Class: 6.1 IMDG Subrisk: None
UN Number: 3249 Packing Group: III
EMS Number: F-A , S-A Special provisions: 221 223
Limited Quantities: 5 kg
Shipping Name: MEDICINE, SOLID, TOXIC, N.O.S.(contains mivacurium hydrochloride)

Section 15 - REGULATORY INFORMATION

No data for mivacurium hydrochloride (CAS: , 106861-44-3)

Section 16 - OTHER INFORMATION

LIMITED EVIDENCE

- Inhalation, skin contact and/or ingestion may produce health damage*.
- Cumulative effects may result following exposure*.
- Possible skin sensitiser*.

* (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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