Atracurium Besylate

sc-210845

Material Safety Data Sheet

Hazard Alert Code Key:	EXTREME	HIGH	MODERATE	LOW

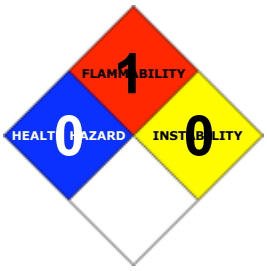
Section 1 - CHEMICAL PRODUCT AND COMPANY IDENTIFICATION

PRODUCT NAME
Atracurium Besylate

STATEMENT OF HAZARDOUS NATURE

CONSIDERED A HAZARDOUS SUBSTANCE ACCORDING TO OSHA 29 CFR 1910.1200.

NFPA



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EMERGENCY
ChemWatch
Within the US & Canada: 877–715–9305
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SYNONYMS
C53H72N2O12.2C6H5O3S, "2, 2' -[1, 5-pentanediylbis(oxy(3-oxo-3, 1-propanediyl))]bis[1-((3, 4-", "dimethoxyphenyl)methyl]-1, 2, 3, 4-tetrahydro-6, 7-dimethoxy-2-", "methylisoquinolinium] dibenzenesulfonate", "2-(2-carboxyethyl)-1, 2, 3, 4-tetrahydro-6, 7-dimethoxy-2-methyl-1-", "veratrylisoquinolinium benzenesulfonate pentamethylene ester", "N, N' -dimethyl-N, N' -(4, 10-dioxa-3, 11-dioxotridecylene)-1, 13-bis-", "tetrahydropapaverinium dibesylate", "isoquinolinium, 2, 2' -(1, 5-pentanediylbis(oxy(3-oxo-3, 1-", "propanediyl)))bis(1-((3, 4-dimethoxyphenyl)methyl)-1, 2, 3, 4-tetrahydro-6, ", "7-dimethoxy-2-methyl-, (1R1' R, 2R, 2' R)-", "cis-atricurium besylate (CAS RN: 96946-42-8)", "cisatricurium besylate", Tracrium, "muscle relaxant"

Section 2 - HAZARDS IDENTIFICATION

CHEMWATCH HAZARD RATINGS

	Min	Max
Flammability:	1	
Toxicity:	2	
Body Contact:	0	
Reactivity:	1	
Chronic:	2	

Min/Nil=0
Low=1
Moderate=2
High=3
Extreme=4

CANADIAN WHMIS SYMBOLS

EMERGENCY OVERVIEW
RISK

POTENTIAL HEALTH EFFECTS

ACUTE HEALTH EFFECTS

SWALLOWED
■ Accidental ingestion of the material may be damaging to the health of the individual.
■ Tubocurarine and its structural analogues rarely produces side-effects at levels employed during anaesthesia but in overdose may cause respiratory failure (by paralysing 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 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.
■ 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
■ 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 benzylisoquinoline 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 benzylisoquinoline compounds used in neuromuscular blockade have a tendency to release histamine, particularly at higher doses.
Although atracurium besylate is a less potent histamine releaser than d-tubocurarine, in common with most neuromuscular blocking agents the potential exists for histamine release in susceptible patients. Adverse reactions include skin flushing, transient hypotension, hypertension,
tachycardia, bradycardia, bronchospasm and anaphylactoid reactions.

Section 3 - COMPOSITION / INFORMATION ON INGREDIENTS

NAME	CAS RN	%
atracurium besylate	64228-81-5	>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 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. · Other measures are usually unnecessary.

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.

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 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 (CO_2), nitrogen oxides (NOx), sulfur oxides (SOx), other pyrolysis products typical of burning organic material.
May emit poisonous fumes.
May emit corrosive 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 at -20° C.
· Store in original containers.
· Keep containers securely sealed.
NOTE: Store in the dark.

Section 8 - EXPOSURE CONTROLS / PERSONAL PROTECTION

EXPOSURE CONTROLS

The following materials had no OELs on our records
• atracurium besylate: CAS:64228-81-5 CAS:96946-42-8

PERSONAL PROTECTION



RESPIRATOR

• particulate.

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

■ 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.
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	1243.49
Melting Range (°F)	185- 194	Viscosity	Not Applicable
Boiling Range (°F)	Not available	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)	>1
Volatile Component (%vol)	Negligible	Evaporation Rate	Not applicable

APPEARANCE

Off-white freeze dried powder; 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

atracurium besylate

TOXICITY AND IRRITATION
ATRACURIUM BESYLATE:
■ unless otherwise specified data extracted from RTECS - Register of Toxic Effects of Chemical Substances.
■ No significant acute toxicological data identified in literature search.
Most neuromuscular blocking agents facilitate histamine release in susceptible patients. Adverse reactions include skin flushing, transient hypotension, hypertension, tachycardia, bradycardia, bronchospasm and anaphylactoid reactions.

For cisatracurium besylate:
Histamine release, hypersensitivity reactions including anaphylactic or anaphylactoid responses which, in rare instances, were severe. There are rare reports of wheezing, laryngospasm, bronchospasm, rash and itching following administration of cisatracurium in children. These reported adverse events were not serious and their etiology could not be established with certainty. Musculoskeletal: Prolonged neuromuscular block, inadequate neuromuscular block, muscle weakness, and myopathy.
Carcinogenesis, Mutagenesis, Impairment of Fertility: Carcinogenesis and fertility studies have not been performed. Cisatracurium besylate was evaluated in a battery of four short-term mutagenicity tests. It was non-mutagenic in the Ames Salmonella assay, a rat bone marrow cytogenetic assay, and an in vitro human lymphocyte cytogenetics assay. As was the case with atracurium, the mouse lymphoma assay was positive both in the presence and absence of exogenous metabolic activation (rat liver S-9). In the absence of S-9, cisatracurium besylate was positive at in vitro cisatracurium concentrations of 40 ug/mL and higher. The highest non-mutagenic concentration (30 ug/mL) and incubation time (4 hours) resulted in an AUC approximately 120 times that noted in clinical studies and approximately 8.5 times the mean peak clinical concentration noted. In the presence of S-9, cisatracurium besylate was positive at a cisatracurium concentration of 300 ug/mL but not at lower or higher concentrations.
Teratology testing in nonventilated pregnant rats treated subcutaneously with maximum subparalysing doses (4 mg/kg daily; equivalent to 8 x the human ED95 following a bolus dose of 0.2 mg/kg IV) and in ventilated rats treated intravenously with paralyzing doses of the drug at 0.5 and 1.0 mg/kg; equivalent to 10 x and 20 x the human ED95 dose, respectively, revealed no maternal or foetal toxicity or teratogenic effects.

Section 12 - ECOLOGICAL INFORMATION

No data

Ecotoxicity

Ingredient	Persistence: Water/Soil	Persistence: Air	Bioaccumulation	Mobility
atracurium besylate	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

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

Section 15 - REGULATORY INFORMATION

No data for atracurium besylate (CAS: , 64228-81-5, 96946-42-8)

Section 16 - OTHER INFORMATION

LIMITED EVIDENCE

■ Ingestion may produce health damage*.
■ Cumulative effects may result following exposure*.
■ Possible skin sensitiser*.
* (limited evidence).

Ingredients with multiple CAS Nos

Ingredient Name CAS atracurium besylate 64228-81-5, 96946-42-8

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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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