Dechra Veterinary Products Tri-Solfen Topical Anaesthetic & Antiseptic Solution For Pain Relief In Lambs & Calves

Dechra Veterinary Products (Australia) Pty Ltd

Chemwatch Hazard Alert Code: **2**

Chemwatch: **923-4599**
Version No: **2.1**
Safety Data Sheet according to WHS Regulations (Hazardous Chemicals) Amendment 2020 and ADG requirements

Issue Date: **24/01/2022**
Print Date: **14/12/2023**
S.GHS.AUS.EN

SECTION 1 Identification of the substance / mixture and of the company / undertaking

Product Identifier

Product name	Dechra Veterinary Products Tri-Solfen Topical Anaesthetic & Antiseptic Solution For Pain Relief In Lambs & Calves
Chemical Name	Not Applicable
Synonyms	TRI-SOLFEN
Chemical formula	Not Applicable
Other means of identification	Not Available

Relevant identified uses of the substance or mixture and uses advised against

Relevant identified uses	Anaesthetic.

Details of the manufacturer or supplier of the safety data sheet

Registered company name	**Dechra Veterinary Products (Australia) Pty Ltd**
Address	2 Cal Close Somersby NSW 2250 Australia
Telephone	(02) 4372 1661|1300 015 825
Fax	(02) 4372 1668
Website	http://www.dechra.com.au/
Email	info.au@dechra.com

Emergency telephone number

Association / Organisation	**Poisons Information Centre**	**CHEMWATCH EMERGENCY RESPONSE (24/7)**
Emergency telephone numbers	13 11 26 (Poisons Information Centre)	+61 1800 951 288
Other emergency telephone numbers	Not Available	+61 3 9573 3188

Once connected and if the message is not in your preferred language then please dial 01

SECTION 2 Hazards identification

Classification of the substance or mixture

Poisons Schedule	S5
Classification [1]	Acute Toxicity (Oral) Category 4, Acute Toxicity (Dermal) Category 4, Skin Corrosion/Irritation Category 2, Serious Eye Damage/Eye Irritation Category 1, Acute Toxicity (Inhalation) Category 4, Germ Cell Mutagenicity Category 2, Hazardous to the Aquatic Environment Long-Term Hazard Category 3
Legend:	*1. Classified by Chemwatch; 2. Classification drawn from HCIS; 3. Classification drawn from Regulation (EU) No 1272/2008 - Annex VI*

Label elements

Hazard pictogram(s)	
Signal word	**Danger**

Hazard statement(s)

H302	Harmful if swallowed.
H312	Harmful in contact with skin.
H315	Causes skin irritation.
H318	Causes serious eye damage.
H332	Harmful if inhaled.
H341	Suspected of causing genetic defects.

Page 1 continued...

H412	Harmful to aquatic life with long lasting effects.
AUH031	Contact with acid liberates toxic gas.

Precautionary statement(s) Prevention

P201	Obtain special instructions before use.
P271	Use only outdoors or in a well-ventilated area.
P280	Wear protective gloves, protective clothing, eye protection and face protection.
P261	Avoid breathing mist/vapours/spray.
P264	Wash all exposed external body areas thoroughly after handling.
P270	Do not eat, drink or smoke when using this product.
P273	Avoid release to the environment.

Precautionary statement(s) Response

P305+P351+P338	IF IN EYES: Rinse cautiously with water for several minutes. Remove contact lenses, if present and easy to do. Continue rinsing.
P308+P313	IF exposed or concerned: Get medical advice/ attention.
P310	Immediately call a POISON CENTER/doctor/physician/first aider.
P301+P312	IF SWALLOWED: Call a POISON CENTER/doctor/physician/first aider if you feel unwell.
P302+P352	IF ON SKIN: Wash with plenty of water.
P304+P340	IF INHALED: Remove person to fresh air and keep comfortable for breathing.
P330	Rinse mouth.
P332+P313	If skin irritation occurs: Get medical advice/attention.
P362+P364	Take off contaminated clothing and wash it before reuse.

Precautionary statement(s) Storage

P405	Store locked up.

Precautionary statement(s) Disposal

P501	Dispose of contents/container to authorised hazardous or special waste collection point in accordance with any local regulation.

SECTION 3 Composition / information on ingredients

Substances

See section below for composition of Mixtures

Mixtures

CAS No	%[weight]	Name
6108-05-0	1-<5	lignocaine hydrochloride
8044-71-1	0.1-0.5	cetrimide
7681-57-4	0.1-<0.5	sodium metabisulfite
14252-80-3	0.1-<0.5	bupivacaine hydrochloride
51-42-3	0.001-<0.005	L-adrenaline-D-hydrogentartrate
Not Available	balance	Ingredients determined not to be hazardous
Legend:	*1. Classified by Chemwatch; 2. Classification drawn from HCIS; 3. Classification drawn from Regulation (EU) No 1272/2008 - Annex VI; 4. Classification drawn from C&L; * EU IOELVs available*	

SECTION 4 First aid measures

Description of first aid measures

Eye Contact	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. ▸ Continue flushing until advised to stop by the Poisons Information Centre or a doctor, or for at least 15 minutes. ▸ Transport to hospital or doctor without delay. ▸ Removal of contact lenses after an eye injury should only be undertaken by skilled personnel.
Skin Contact	If skin contact occurs: ▸ Immediately remove all contaminated clothing, including footwear. ▸ Flush skin and hair with running water (and soap if available). ▸ Seek medical attention in event of irritation.
Inhalation	▸ If fumes or combustion products are inhaled remove from contaminated area. ▸ Lay patient down. Keep warm and rested. ▸ Prostheses such as false teeth, which may block airway, should be removed, where possible, prior to initiating first aid procedures. ▸ Apply artificial respiration if not breathing, preferably with a demand valve resuscitator, bag-valve mask device, or pocket mask as trained. Perform CPR if necessary. ▸ Transport to hospital, or doctor, without delay.

Continued...

Ingestion	▸ **IF SWALLOWED, REFER FOR MEDICAL ATTENTION, WHERE POSSIBLE, WITHOUT DELAY.** ▸ For advice, contact a Poisons Information Centre or a doctor. ▸ Urgent hospital treatment is likely to be needed. ▸ In the mean time, qualified first-aid personnel should treat the patient following observation and employing supportive measures as indicated by the patient's condition. ▸ If the services of a medical officer or medical doctor are readily available, the patient should be placed in his/her care and a copy of the SDS should be provided. Further action will be the responsibility of the medical specialist. ▸ If medical attention is not available on the worksite or surroundings send the patient to a hospital together with a copy of the SDS. **Where medical attention is not immediately available or where the patient is more than 15 minutes from a hospital or unless instructed otherwise:** ▸ **INDUCE** vomiting with fingers down the back of the throat, **ONLY IF CONSCIOUS**. Lean patient forward or place on left side (head-down position, if possible) to maintain open airway and prevent aspiration. **NOTE:** Wear a protective glove when inducing vomiting by mechanical means.

Indication of any immediate medical attention and special treatment needed

When systemic reaction to local anaesthetic occurs, steps should be taken to maintain circulation and respiration and control convulsions. A clear airway should be established and oxygen given together with assisted ventilation if necessary. Circulation should be maintained with plasma infusion (or suitable electrolytes). Vasopressors such as ephedrine, metaraminol and methoxamine have been suggested in marked hypotension although their use is accompanied by the risk of CNS excitement. (Vasopressors should not be given in patients receiving oxytocic drugs.) Convulsions may be controlled by the use of diazepam or short acting barbiturates such as thiopentone sodium. It should be remembered that anticonvulsant treatment may also depress respiration. A short-acting neuromuscular blocking agent, together with endotracheal intubation and artificial respiration has been used when convulsions persist.
Methaemoglobinaemia may be treated by intravenous administration of a 1% solution of methylene blue.
MARTINDALE; The Extra Pharmacopoeia, 29th Edition
Local anaesthetics produce vasodilation by blocking sympathetic nerves. Elevating the patient's legs and positioning the patient on the left side will help decrease blood pressure.
Metabolism of amide-type anaesthetics occurs in the liver and in some cases in the kidney. Because these undergo extensive and rapid hepatic metabolism, only about 1/3 of an oral dose reaches the systemic circulation.

SECTION 5 Firefighting measures

Extinguishing media

▸ There is no restriction on the type of extinguisher which may be used.
▸ Use extinguishing media suitable for surrounding area.

Special hazards arising from the substrate or mixture

Fire Incompatibility	▸ Avoid contamination with oxidising agents i.e. nitrates, oxidising acids, chlorine bleaches, pool chlorine etc. as ignition may result

Advice for firefighters

Fire Fighting	▸ Alert Fire Brigade and tell them location and nature of hazard. ▸ Wear breathing apparatus plus protective gloves in the event of a fire. ▸ Prevent, by any means available, spillage from entering drains or water courses. ▸ Use fire fighting procedures suitable for surrounding area. ▸ **DO NOT** approach containers suspected to be hot. ▸ Cool fire exposed containers with water spray from a protected location. ▸ If safe to do so, remove containers from path of fire. ▸ Equipment should be thoroughly decontaminated after use.
Fire/Explosion Hazard	carbon dioxide (CO_2) hydrogen bromide nitrogen oxides (NO_x) sulfur oxides (SO_x) other pyrolysis products typical of burning organic material. May emit poisonous fumes. May emit corrosive fumes. ▸ Non combustible. ▸ Not considered a significant fire risk, however containers may burn. Decomposes on heating and produces: carbon monoxide (CO)
HAZCHEM	Not Applicable

SECTION 6 Accidental release measures

Personal precautions, protective equipment and emergency procedures

See section 8

Environmental precautions

See section 12

Methods and material for containment and cleaning up

Minor Spills	▸ Clean up all spills immediately. ▸ Avoid breathing vapours and contact with skin and eyes. ▸ Control personal contact with the substance, by using protective equipment. ▸ Contain and absorb spill with sand, earth, inert material or vermiculite. ▸ Wipe up. ▸ Place in a suitable, labelled container for waste disposal.
Major Spills	Moderate hazard. ▸ Clear area of personnel and move upwind. ▸ Alert Fire Brigade and tell them location and nature of hazard.

Continued...

	▸ Wear breathing apparatus plus protective gloves. ▸ Prevent, by any means available, spillage from entering drains or water course. ▸ Stop leak if safe to do so. ▸ Contain spill with sand, earth or vermiculite. ▸ Collect recoverable product into labelled containers for recycling. ▸ Neutralise/decontaminate residue (see Section 13 for specific agent). ▸ Collect solid residues and seal in labelled drums for disposal. ▸ Wash area and prevent runoff into drains. ▸ After clean up operations, decontaminate and launder all protective clothing and equipment before storing and re-using. ▸ If contamination of drains or waterways occurs, advise emergency services.

Personal Protective Equipment advice is contained in Section 8 of the SDS.

SECTION 7 Handling and storage

Precautions for safe handling

Safe handling	▸ **DO NOT** allow clothing wet with material to stay in contact with skin ▸ Avoid all personal contact, including inhalation. ▸ Wear protective clothing when risk of exposure occurs. ▸ Use in a well-ventilated area. ▸ Avoid contact with moisture. ▸ Avoid contact with incompatible materials. ▸ When handling, **DO NOT** eat, drink or smoke. ▸ Keep containers securely sealed when not in use. ▸ Avoid physical damage to containers. ▸ Always wash hands with soap and water after handling. ▸ Work clothes should be laundered separately. Launder contaminated clothing before re-use. ▸ Use good occupational work practice. ▸ Observe manufacturer's storage and handling recommendations contained within this SDS. ▸ Atmosphere should be regularly checked against established exposure standards to ensure safe working conditions are maintained.
Other information	▸ Store in original containers. ▸ Keep containers securely sealed. ▸ Store in a cool, dry, well-ventilated area. ▸ Store away from incompatible materials and foodstuff containers. ▸ Protect containers against physical damage and check regularly for leaks. ▸ Observe manufacturer's storage and handling recommendations contained within this SDS.

Conditions for safe storage, including any incompatibilities

Suitable container	▸ Glass container is suitable for laboratory quantities ▸ Polyethylene or polypropylene container. ▸ Packing as recommended by manufacturer. ▸ Check all containers are clearly labelled and free from leaks.
Storage incompatibility	▸ Contact with acids produces toxic fumes ▸ Avoid reaction with oxidising agents

SECTION 8 Exposure controls / personal protection

Control parameters

Occupational Exposure Limits (OEL)

INGREDIENT DATA

Source	Ingredient	Material name	TWA	STEL	Peak	Notes
Australia Exposure Standards	sodium metabisulfite	Sodium metabisulphite	5 mg/m3	Not Available	Not Available	Not Available

Emergency Limits

Ingredient	TEEL-1	TEEL-2	TEEL-3
sodium metabisulfite	15 mg/m3	64 mg/m3	390 mg/m3

Ingredient	Original IDLH	Revised IDLH
lignocaine hydrochloride	Not Available	Not Available
cetrimide	Not Available	Not Available
sodium metabisulfite	Not Available	Not Available
bupivacaine hydrochloride	Not Available	Not Available
L-adrenaline-D-hydrogentartrate	Not Available	Not Available

Occupational Exposure Banding

Ingredient	Occupational Exposure Band Rating	Occupational Exposure Band Limit
lignocaine hydrochloride	E	≤ 0.01 mg/m³
cetrimide	C	> 0.1 to ≤ milligrams per cubic meter of air (mg/m³)
bupivacaine hydrochloride	D	> 0.01 to ≤ 0.1 mg/m³
L-adrenaline-D-hydrogentartrate	E	≤ 0.01 mg/m³
Notes:	*Occupational exposure banding is a process of assigning chemicals into specific categories or bands based on a chemical's potency and the adverse health outcomes associated with exposure. The output of this process is an occupational exposure band (OEB), which corresponds to a range of exposure concentrations that are expected to protect worker health.*	

Continued...

Exposure controls

Appropriate engineering controls	**Unless written procedures, specific to the workplace are available, the following is intended as a guide:** ▸ **For Laboratory-scale handling of Substances assessed to be toxic by inhalation. *Quantities of up to 25 grams*** may be handled in Class II biological safety cabinets *; ***Quantities of 25 grams to 1 kilogram*** may be handled in Class II biological safety cabinets* or equivalent containment systems; ***Quantities exceeding 1 kg*** may be handled either using specific containment, a hood or Class II biological safety cabinet*, ▸ HEPA terminated local exhaust ventilation should be considered at point of generation of dust, fumes or vapours. ▸ The need for respiratory protection should also be assessed where incidental or accidental exposure is anticipated. Dependent on levels of contamination, PAPR, full face air purifying devices with P2 or P3 filters or air supplied respirators should be evaluated. When handling: ***Quantities of up to 25 grams***, an approved respirator with HEPA filters or cartridges should be considered; ***Quantities of 25 grams to 1 kilogram,*** a half-face negative pressure, full negative pressure, or powered helmet-type air purifying respirator should be considered. ***Quantities in excess of 1 kilogram*****,** a full face negative pressure, helmet-type air purifying, or supplied air respirator should be considered. Written procedures, specific to a particular work-place, may replace these recommendations * For Class II Biological Safety Cabinets, Types B2 or B3 should be considered. Where only Class I, open fronted Cabinets are available, glove panels may be added, Laminar flow cabinets do not provide sufficient protection when handling these materials unless especially designed to do so. **Pilot Plant and Production** ▸ Wear appropriate gloves; lab coat, nylon coveralls or disposable Tyvek suit; safety glasses, safety shoes, and disposable booties. Use good manufacturing practices (i.e., cGMPs). ▸ Protective garment (coveralls, Tyvek, lab coat) is not to be worn outside the work area. ▸ Clean/dirty/decontamination areas are to be established. ▸ Negative/positive air pressure relationships and buffer zones required (i.e., ante-room/degowning room/airlock). ▸ Area access is to be restricted. ▸ High-energy operations such as milling, particle sizing, spraying or fluidising should be done within an approved emission control or containment system. ▸ Develop cleaning procedures and techniques that limit potential exposure **For potent pharmacological agents:** **Solutions Handling:** ▸ Solutions can be handled outside a containment system or without local exhaust ventilation during procedures with no potential for aerosolisation. If the procedures have a potential for aerosolisation, an air-purifying respirator is to be worn by all personnel in the immediate area. ▸ Solutions used for procedures where aerosolisation may occur (e.g., vortexing, pumping) are to be handled within a containment system or with local exhaust ventilation. ▸ In situations where this is not feasible (may include animal dosing), an air-purifying respirator is to be worn by all personnel in the immediate area. If using a ventilated enclosure that has not been validated, wear a half-mask respirator equipped with HEPA cartridges until the enclosure is validated for use. ▸ Ensure gloves are protective against solvents in use.
Individual protection measures, such as personal protective equipment	
Eye and face protection	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. [AS/NZS 1337.1, EN166 or national equivalent] ▸ 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 lenses 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].
Skin protection	See Hand protection below
Hands/feet protection	**NOTE:** ▸ The material may produce skin sensitisation in predisposed individuals. Care must be taken, when removing gloves and other protective equipment, to avoid all possible skin contact. ▸ Contaminated leather items, such as shoes, belts and watch-bands should be removed and destroyed. The selection of suitable gloves does not only depend on the material, but also on further marks of quality which vary from manufacturer to manufacturer. Where the chemical is a preparation of several substances, the resistance of the glove material can not be calculated in advance and has therefore to be checked prior to the application. The exact break through time for substances has to be obtained from the manufacturer of the protective gloves and has to be observed when making a final choice. Personal hygiene is a key element of effective hand care. 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. Suitability and durability of glove type is dependent on usage. Important factors in the selection of gloves include: · 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, AS/NZS 2161.1 or national equivalent). · 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, AS/NZS 2161.10.1 or national equivalent) 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, AS/NZS 2161.10.1 or national equivalent) is recommended. · Some glove polymer types are less affected by movement and this should be taken into account when considering gloves for long-term use. · Contaminated gloves should be replaced. As defined in ASTM F-739-96 in any application, gloves are rated as: · Excellent when breakthrough time > 480 min · Good when breakthrough time > 20 min · Fair when breakthrough time < 20 min · Poor when glove material degrades For general applications, gloves with a thickness typically greater than 0.35 mm, are recommended. It should be emphasised that glove thickness is not necessarily a good predictor of glove resistance to a specific chemical, as the permeation efficiency of the glove will be dependent on the exact composition of the glove material. Therefore, glove selection should also be based on

Continued...

	consideration of the task requirements and knowledge of breakthrough times. Glove thickness may also vary depending on the glove manufacturer, the glove type and the glove model. Therefore, the manufacturers technical data should always be taken into account to ensure selection of the most appropriate glove for the task. Note: Depending on the activity being conducted, gloves of varying thickness may be required for specific tasks. For example: · Thinner gloves (down to 0.1 mm or less) may be required where a high degree of manual dexterity is needed. However, these gloves are only likely to give short duration protection and would normally be just for single use applications, then disposed of. · Thicker gloves (up to 3 mm or more) may be required where there is a mechanical (as well as a chemical) risk i.e. where there is abrasion or puncture potential 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, latex/ nitrile). Employees allergic to latex gloves should use nitrile gloves in preference. ▸ Double gloving should be considered. ▸ PVC gloves. ▸ Change gloves frequently and when contaminated, punctured or torn. ▸ Wash hands immediately after removing gloves. ▸ Protective shoe covers. [AS/NZS 2210] ▸ Head covering.
Body protection	See Other protection below
Other protection	▸ 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

Respiratory protection

Type A Filter of sufficient capacity. (AS/NZS 1716 & 1715, EN 143:2000 & 149:2001, ANSI Z88 or national equivalent)

Where the concentration of gas/particulates in the breathing zone, approaches or exceeds the "Exposure Standard" (or ES), respiratory protection is required.
Degree of protection varies with both face-piece and Class of filter; the nature of protection varies with Type of filter.

Required Minimum Protection Factor	Half-Face Respirator	Full-Face Respirator	Powered Air Respirator
up to 10 x ES	A-AUS	-	A-PAPR-AUS / Class 1
up to 50 x ES	-	A-AUS / Class 1	-
up to 100 x ES	-	A-2	A-PAPR-2 ^

^ - Full-face
A(All classes) = Organic vapours, B AUS or B1 = Acid gasses, B2 = Acid gas or hydrogen cyanide(HCN), B3 = Acid gas or hydrogen cyanide(HCN), E = Sulfur dioxide(SO2), G = Agricultural chemicals, K = Ammonia(NH3), Hg = Mercury, NO = Oxides of nitrogen, MB = Methyl bromide, AX = Low boiling point organic compounds(below 65 degC)

- Cartridge respirators should never be used for emergency ingress or in areas of unknown vapour concentrations or oxygen content.
- The wearer must be warned to leave the contaminated area immediately on detecting any odours through the respirator. The odour may indicate that the mask is not functioning properly, that the vapour concentration is too high, or that the mask is not properly fitted. Because of these limitations, only restricted use of cartridge respirators is considered appropriate.
- Cartridge performance is affected by humidity. Cartridges should be changed after 2 hr of continuous use unless it is determined that the humidity is less than 75%, in which case, cartridges can be used for 4 hr. Used cartridges should be discarded daily, regardless of the length of time used

SECTION 9 Physical and chemical properties

Information on basic physical and chemical properties

Appearance	Blue liquid with slight odour; mixes with water.

Physical state	Liquid	**Relative density (Water = 1)**	1.03
Odour	Not Available	**Partition coefficient n-octanol / water**	Not Available
Odour threshold	Not Available	**Auto-ignition temperature (°C)**	Not Applicable
pH (as supplied)	2-3	**Decomposition temperature (°C)**	Not Available
Melting point / freezing point (°C)	Not Available	**Viscosity (cSt)**	~276.699
Initial boiling point and boiling range (°C)	>100	**Molecular weight (g/mol)**	Not Applicable
Flash point (°C)	Not Applicable	**Taste**	Not Available
Evaporation rate	Not Available	**Explosive properties**	Not Available
Flammability	Not Applicable	**Oxidising properties**	Not Available
Upper Explosive Limit (%)	Not Applicable	**Surface Tension (dyn/cm or mN/m)**	Not Available
Lower Explosive Limit (%)	Not Applicable	**Volatile Component (%vol)**	Not Available
Vapour pressure (kPa)	Not Available	**Gas group**	Not Available
Solubility in water	Miscible	**pH as a solution (1%)**	Not Available
Vapour density (Air = 1)	Not Available	**VOC g/L**	Not Available

SECTION 10 Stability and reactivity

Continued...

Reactivity	See section 7
Chemical stability	▸ Unstable in the presence of incompatible materials. ▸ Product is considered stable. ▸ Hazardous polymerisation will not occur.
Possibility of hazardous reactions	See section 7
Conditions to avoid	See section 7
Incompatible materials	See section 7
Hazardous decomposition products	See section 5

SECTION 11 Toxicological information

Information on toxicological effects

Inhaled	The material can cause respiratory irritation in some persons. The body's response to such irritation can cause further lung damage. Inhalation of local anaesthetics may result in upper respiratory tract effects including burning sensation, stinging, tenderness, swelling, sloughing, tissue necrosis and irritation. Systemic poisoning is characterised by lightheadedness, nervousness, apprehension, euphoria, confusion, dizziness, drowsiness, tinnitus, blurred or double vision, vomiting and sensations of heat, cold or numbness, twitching, tremors, convulsions, unconsciousness and respiratory depression and arrest. Inhalation of vapours or aerosols (mists, fumes), generated by the material during the course of normal handling, may be harmful.
Ingestion	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. Systemic toxicity due to local anaesthetics may be manifested by yawning, restlessness, excitement, ringing sound in the ear, nausea and vomiting. Early warning signs are numbness of the tongue and around the mouth region.
Skin Contact	Skin contact with the material may be harmful; systemic effects may result following absorption. This material can cause inflammation of the skin on contact in some persons. The material may accentuate any pre-existing dermatitis condition Repeated exposure may cause skin cracking, flaking or drying following normal handling and use. When applied to the skin, local anaesthetics can cause burning, stinging, tenderness, redness, sloughing, blisters and tissue death. There may be skin eruptions caused by simultaneous exposure to light. 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.
Eye	If applied to the eyes, this material causes severe eye damage. Direct eye contact with local anaesthetics may reduce sensation in the eyes and increase the risk of injury due to foreign bodies. There may be drying of the cornea, a burning sensation, excessive tears, sensitivity to light, swelling and redness of the conjunctiva and increased blinking. Absorption into the body can cause degeneration of the optic nerve, leading to blindness.
Chronic	There has been concern that this material can cause cancer or mutations, but there is not enough data to make an assessment. Repeated or long-term occupational exposure is likely to produce cumulative health effects involving organs or biochemical systems. Long-term exposure to respiratory irritants may result in airways disease, involving difficulty breathing and related whole-body problems. Inhaling this product is more likely to cause a sensitisation reaction in some persons compared to the general population. Skin contact with the material is more likely to cause a sensitisation reaction in some persons compared to the general population. Harmful: danger of serious damage to health by prolonged exposure through inhalation, in contact with skin and if swallowed. This material can cause serious damage if one is exposed to it for long periods. It can be assumed that it contains a substance which can produce severe defects. There is some evidence from animal testing that exposure to this material may result in toxic effects to the unborn baby. Repeated or prolonged exposure with local anaesthetics may result in sensitization of skin, with the development of lesions, hives and oedema. There may be anaphylactic reactions that may cause death. Chronic poisoning from ionic bromides has historically resulted from medical use of bromides but not from exposure in the environment or workplace. In the absence of other signs of poisoning, there may be depression, hallucinations and schizophrenia-like psychosis. Bromides may also cause sedation, irritability, agitation, delirium, memory loss, confusion, disorientation, forgetfulness, inability to speak, difficulty speaking, weakness, fatigue, a spinning sensation, stupor, coma, decreased appetite, nausea, vomiting, an acne-like rash on the face (bronchoderma), legs and trunk, swelling of the bronchi and a profuse discharge from the nostrils. There may also be inco-ordination and very brisk reflexes. Correlation of nervous system symptoms with blood levels of bromide is inexact. Current day usage of bromides is generally limited to antihistamines such as brompheniramine, which is a covalent compound; ionic compounds are no longer regularly used due to their toxicity. In test animals, brominated vegetable oils (BVOs), historically used as emulsifiers in certain soda-based soft drinks, produced damage to the heart and kidneys in addition to increasing fat deposits in these organs. In extreme cases, BVOs caused testicular damage, stunted growth and produced lethargy and fatigue. Brominism (chronic bromine poisoning) produces slurred speech, apathy, headache, decreased memory, anorexia and drowsiness, psychosis resembling paranoid schizophrenia, and personality changes. Several cases of foetal abnormalities have been described in mothers who took large doses of bromides during pregnancy. Reproductive effects caused by bromide (which crosses the placenta) include central nervous system depression, brominism, and bronchoderma (an acne-like rash) in the newborn.

Dechra Veterinary Products Tri-Solfen Topical Anaesthetic & Antiseptic Solution For Pain Relief In Lambs & Calves	**TOXICITY**	**IRRITATION**
	Not Available	Not Available
lignocaine hydrochloride	**TOXICITY**	**IRRITATION**
	Oral (Mouse) LD50; 292 mg/kg[2]	Not Available
cetrimide	**TOXICITY**	**IRRITATION**
	Not Available	Eye: SEVERE
sodium metabisulfite	**TOXICITY**	**IRRITATION**
	dermal (rat) LD50: >2000 mg/kg[1]	Eye (rabbit): IRRITANT **CCInfo. No. 1478367 [BASF] [ICI UK] [Sigma/Aldrich]

Continued...

	Oral (Rat) LD50: 500 mg/kg[2]	
bupivacaine hydrochloride	**TOXICITY**	**IRRITATION**
	Oral (Rabbit) LD50; 18 mg/kg[2]	Not Available
L-adrenaline-D-hydrogentartrate	**TOXICITY**	**IRRITATION**
	Oral (Mouse) LD50; 4 mg/kg[2]	Not Available

Legend:	*1. Value obtained from Europe ECHA Registered Substances - Acute toxicity 2. Value obtained from manufacturer's SDS. Unless otherwise specified data extracted from RTECS - Register of Toxic Effect of chemical Substances*

LIGNOCAINE HYDROCHLORIDE	Laboratory (in vitro) and animal studies show, exposure to the material may result in a possible risk of irreversible effects, with the possibility of producing mutation. The material may cause skin irritation after prolonged or repeated exposure and may produce on contact skin redness, swelling, the production of vesicles, scaling and thickening of the skin.
CETRIMIDE	Oral (rat) Median Lethal Dose 1000 mg/kg [Manufacturer] For alkyltrimethylammonium chloride (ATMAC) Most undiluted cationic surfactants satisfy the criteria for classification as Harmful (Xn) with R22 and as Irritant (Xi) for skin and eyes with R38 and R41. In addition, certain surfactants will satisfy the criteria for classification as Corrosive with R34 in addition to the acute toxicity. According to Centre Europeen des Agents de Surface et de leurs Intermediaires Organiques (CESIO), C8-18 alkyltrimethylammonium chloride (ATMAC) (i.e., lauryl, coco, soya, and tallow) are classified as Corrosive (C) with the risk phrases R22 (Harmful if swallowed) and R34 (Causes burns). C16 ATMAC is classified as Harmful (Xn) with the risk phrases R22 (Harmful if swallowed), R38 (Irritating to skin), and R41 (Risk of serious damage to eyes). C20-22 ATMAC are classified as Irritant (Xi) with R36/38 (Irritating to eyes and skin). Acute toxicity: ATMAB (the bromide) is poorly absorbed through the skin or the digestive tract. Acute oral toxicity of alkyltrimethylammonium salts is somewhat higher than the toxicity of anionic and nonionic surfactants. This may be due to the strongly irritating effect which cationic surfactants have on the mucous membrane of the gastrointestinal tract. Cationic surfactants are generally about 10 times more toxic when given through a vein, compared to being given by mouth. Skin and eye irritation: Skin irritation depends on surfactant concentration. Concentrations above 1% generally cause pronounced irritation. Cationic surfactants are the most irritating surfactants to the eye. Many proteins in the skin are considerably more resistant to the denaturing effects of cationic surfactants compared to those of anionic surfactants. In contrast to the irreversible denaturing effect of sodium dodecyl sulfate, the adverse effects of some cationic surfactants on proteins may be reversible. Sensitisation: A repeated patch test performed on human volunteers did not show sensitization. Sub-chronic toxicity: Animal testing over the long term resulted in no affects, except for reduced body weight at very high doses. Reproductive toxicity: Animal testing showed no effects toxic to the embryo or causing birth defects. Mild effects on the embryo were seen only at levels which were toxic to the mother. Mutation-causing potential: Animal testing showed no mutation-causing potential for C16 and C18 ATMAC. For quaternary ammonium compounds (QACs): Quaternary ammonium compounds (QACs) are cationic surfactants. They are in general more toxic than anionic and non-ionic surfactants. Because they can dissolve phospholipids and cholesterol in lipid membranes, QACs affect cell permeability which may lead to cell death. Further, QACs denature proteins as cationic materials precipitate protein and are accompanied by generalized tissue irritation. It has been suggested that the experimentally determined decrease in the acute toxicity of QAs with chain length above C16 is due to decreased water solubility. In general it appears that QACs with single long-chain alkyl groups are more toxic and irritating than those with two such substitutions. Animal testing shows that straight chain aliphathic QACs may cause lung tissue to release histamine. QACs may also show curare-like properties, causing limb paralysis and even life-threatening paralysis of the muscles of breathing, if they are injected. This paralysis seems to be transient. From human testing, it is concluded that all the compounds investigated to date show similar toxicological properties. The material may produce severe irritation to the eye causing pronounced inflammation. Repeated or prolonged exposure to irritants may produce conjunctivitis.
SODIUM METABISULFITE	The substance is classified by IARC as Group 3: **NOT** classifiable as to its carcinogenicity to humans. Evidence of carcinogenicity may be inadequate or limited in animal testing.
BUPIVACAINE HYDROCHLORIDE	Anticonvulsant properties, somnolence recorded. The following information refers to contact allergens as a group and may not be specific to this product. Contact allergies quickly manifest themselves as contact eczema, more rarely as urticaria or Quincke's oedema. The pathogenesis of contact eczema involves a cell-mediated (T lymphocytes) immune reaction of the delayed type. Other allergic skin reactions, e.g. contact urticaria, involve antibody-mediated immune reactions. The significance of the contact allergen is not simply determined by its sensitisation potential: the distribution of the substance and the opportunities for contact with it are equally important. A weakly sensitising substance which is widely distributed can be a more important allergen than one with stronger sensitising potential with which few individuals come into contact. From a clinical point of view, substances are noteworthy if they produce an allergic test reaction in more than 1% of the persons tested. Medications that act by sodium channel blockade have a wide variety of clinical applications. Broadly they include Vaughn Williams Class 1 antiarrhythmics, local anesthetics, many medications used to treat neuropathic pain (including tricyclic antidepressants (TCA)), anticonvulsants, and cocaine. Insecticides also cause sodium channel blockade. Toxicity of all these substances, whether intentional or accidental, can lead to catastrophic effects including death. It is essential to understand how these medications work, in order to effectively treat their toxicity and side effects. Sodium channel blocker toxicity results primarily from intentional overdose. Broadly speaking, sodium channel blockers cause metabolic, cardiac, and neurologic symptoms. This leads to haemodynamic compromise and metabolic acidosis, potentiating the effects of the medications and causing further sodium blockade. Sodium channel blockers cross the blood-brain barrier and act through multiple mechanisms. They inhibit the gamma-aminobutyric acid (GABA) system (primarily lidocaine), activate the sodium ouabain-sensitive current, stimulate 5-TH2C receptors, antagonize H1 receptors and block all noradrenaline activating effect. It is through these actions that adrenergic stimulation occurs. These medications in large doses are also pro-convulsant through the above mechanisms. TCAs are well known for their concomitant anticholinergic effects but they also produce potassium channel blockade, peripheral alpha blockade, and norepinephrine reuptake blockade, all of which will potentially cloud the clinical presentation. The anticholinergic effects of IA drugs can produce tachycardia, dry mouth, urinary retention, blurred vision and constipation.
L-ADRENALINE-D-HYDROGENTARTRATE	Reproductive effector Adverse reactions to adrenaline include palpitations, tachycardia, arrhythmia, anxiety, panic attack, headache, tremor, hypertension, and acute pulmonary edema. The use of adrenaline (epinephrine)- based eye-drops, commonly used to treat glaucoma, may also lead to buildup of adrenochrome pigments in the conjunctiva, iris, lens, and retina. Rarely, exposure to medically administered epinephrine may cause Takotsubo cardiomyopathy.

Continued...

Use is contraindicated in people on nonselective beta-blockers, because severe hypertension and even cerebral hemorrhage may result.
For beta adrenoreceptor agonists
A major side effect of beta-agonists is cardiac arrhythmia. Because these drugs increase myocardial oxygen demand, they can precipitate angina in patients with coronary artery disease. Headache and tremor are also common.
Beta-adrenoceptor agonists (beta-agonists) bind to beta-receptors on cardiac and smooth muscle tissues. They also have important actions in other tissues, especially bronchial smooth muscle (relaxation), the liver (stimulate glycogenolysis) and kidneys (stimulate renin release).
Beta-adrenoceptors normally bind to norepinephrine released by sympathetic adrenergic nerves, and to circulating epinephrine. Therefore, beta-agonists mimic the actions of sympathetic adrenergic stimulation acting through ß-adrenoceptors. Overall, the effect of beta-agonists is cardiac stimulation (increased heart rate, contractility, conduction velocity, relaxation) and systemic vasodilation. Arterial pressure may increase, but not necessarily because the fall in systemic vascular resistance offsets the increase in cardiac output. Therefore, the effect on arterial pressure depends on the relative influence on cardiac versus vascular beta-adrenoceptors. Long-term exposure to beta-agonists can cause beta-receptor down-regulation, which limits their therapeutic efficacy to short-term application. Beta-agonists, because they are catecholamines, have a low bioavailability and therefore must be given by intravenous infusion.
beta2-Agonists,lowers potassium levels and raises glucose levels, so there is a risk of exacerbating hypokalaemia or hyperglycaemia.
There are several different beta-agonists that are used clinically for the treatment of heart failure or circulatory shock, all of which are either natural catecholamines or analogs. Nearly all of these beta-agonists, however, have some degree of alpha-agonist activity.
Subtype unspecific beta adrenoreceptor agonists can be used to treat:
heart failure – increase cardiac output acutely in an emergency, circulatory shock – increase cardiac output thus redistributing blood volume, anaphylaxis – bronchodilation
Excessive beta-adrenergic stimulation has been associated with seizures, angina, hypertension or hypotension, tachycardia with rates up to 200 beats/min, arrhythmias, nervousness, headache, tremor, palpitation, nausea, dizziness, fatigue, malaise, and insomnia.
In addition, beta-agonists have been reported to produce electrocardiogram (ECG) changes, such as flattening of the T wave, prolongation of the QTc interval, and ST segment depression. The clinical significance of these findings is unknown.
Beta-adrenergic agonist medicines may produce significant hypokalemia in some patients, possibly through intracellular shunting, which has the potential to produce adverse cardiovascular effects.
Fetal toxic effects characteristically observed following beta-adrenoceptor stimulation. These included precocious eyelid openings, cleft palate, sternebral fusion, limb and paw flexures, and delayed ossification of the frontal cranial bones.
Ossification effects are often exhibited by beta-2-agonists and occur at maternal levels substantially higher than those which occur with therapeutic use
Smooth muscle tumours in rats and mice are thought to result from chronic stimulation of beta-adrenoreceptors in the tissues.
Diverse stimuli activate the sympathetic nervous system, leading to increased levels of catecholamines. Long-term overstimulation of the beta-adrenergic receptor (betaAR) in response to catecholamines causes cardiovascular diseases, including cardiac hypertrophy, stroke, coronary artery disease, and heart failure. Although catecholamines have identical sites of action in the heart and cerebral artery, the structural and functional modifications differentially activate intracellular signaling cascades. betaAR-stimulation can increase oxidative stress in the heart and cerebral artery, but has also been shown to induce different cytoskeletal and functional modifications by modulating various components of the betaAR signal transduction pathways. Stimulation of betaAR leads to cardiac dysfunction due to an overload of intracellular Ca2+ in cardiomyocytes. However, this stimulation induces vascular dysfunction through disruption of actin cytoskeleton in vascular smooth muscle cells. Many studies have shown that excessive concentrations of catecholamines during stressful conditions can produce coronary spasms or arrhythmias by inducing Ca2+-handling abnormalities and impairing energy production in mitochondria, In this article, we highlight the different fates caused by excessive oxidative stress and disruptions in the cytoskeletal proteome network in the heart and the cerebral artery in responsed to prolonged betaAR-stimulation.
The pharmacologic effects of beta adrenergic agonist drugs are at least in part attributable to stimulation through beta adrenergic receptors of intracellular adenyl cyclase, the enzyme which catalyzes the conversion of adenosine triphosphate (ATP) to cyclic-3',5'-adenosine monophosphate (c-AMP). Increased c-AMP levels are associated with relaxation of bronchial smooth muscle and inhibition of release of mediators of immediate hypersensitivity from cells, especially from mast cells.
Several studies in laboratory animals (minipigs, rodents and dogs) recorded the occurrence of cardiac arrhythmias and sudden death (with histologic evidence of myocardial necrosis) when beta agonists and methylxanthines were administered concurrently. The significance of these findings when applied to humans is currently unknown.
The benefits of beta-2 agonists on the overall effect against mortality and morbidity have been a widely debated topic of discussion. While long-acting beta agonists (LABAs) have been proven to improve pulmonary function, provide symptomatic relief, and improve quality of life, data suggests that the chronic use of LABAs as a monotherapy approach has led to an overall increase in severe asthma incidences up to hospitalization, intubation, or even mortality. Subsequent studies were performed using dual therapy of LABAs and inhaled corticosteroid (ICS) as a treatment for asthma, and, compared to monotherapy, there was a decrease in the incidence of severe asthma exacerbations
Current literature continues to support the safety of dual therapy versus monotherapy. In 2017, the FDA approved the safety of dual therapy in asthmatic patients while warning against the use of monotherapy of LABAs. The Global Initiative for COPD and National Asthma Education and Prevention, as well as many other guidelines which are in agreement regarding dual therapy to treat asthma uncontrolled with short acting beta agonist (SABA). Despite the support, it is still unclear whether dual therapy can provide complete protection against the risk of asthma exacerbations historically correlated with single LABA treatment.
The topic of SABA overuse in previously clinically stable COPD patients is a point of discussion as studies have demonstrated without conclusive evidence a worsening of disease severity in this setting. An increase in airway hyperreactivity seems to occur with frequent, consistent usage of SABAs, which potentially lead to paradoxical airway narrowing. SABA overuse is relatively prevalent in the population of asthma and COPD patients. In a study on COPD patients currently on treatment, 19% were overusing SABAs, and a separate study on asthmatic patients showed 15.8% overuse of SABAs. In COPD patients, there was an association with increased dyspnea and worsening of quality of life.
For beta adrenoreceptor antagonists
Subtype unspecific beta antagonists (beta blockers) can be used to treat:
heart arrhythmia – decrease the output of sinus node thus stabilizing heart function, coronary artery disease – reduce heart rate and hence increasing oxygen supply, heart failure – prevent sudden death related to this condition, which is often caused by ischemias or arrhythmias, hyperthyroidism – reduce peripheral sympathetic hyperresponsiveness, migraine –reduce number of attacks, stage fright – reduce tachycardia and tremor, glaucoma – reduce intraocular pressure.
Beta blockers can cause depression of myocardial contractility and may precipitate heart failure and cardiogenic shock. Patients with bronchospastic disease, should, in general, not receive beta blockers.
Beta blockers may mask tachycardia occurring with hypoglycemia, but other manifestations such as dizziness and sweating may not be significantly affected.
Beta-adrenergic blockade may mask certain clinical signs (e.g., tachycardia) of hyperthyroidism
In patients with latent cardiac insufficiency, continued depression of the myocardium with beta-blocking agents over a period of time can in some cases lead to cardiac failure. At the first sign or symptom of impending cardiac failure, patients should be fully digitalized and/or be given a diuretic, and the response observed closely.
While taking beta blockers, patients with a history of severe anaphylactic reaction to a variety of allergens may be more reactive to repeated challenge, either accidental, diagnostic, or therapeutic. Such patients may be unresponsive to the usual doses of epinephrine used to treat allergic reaction.
Hypersensitivity to catecholamines has been observed in patients withdrawn from beta-blocker therapy; exacerbation of angina and, in some cases, myocardial infarction have occurred after abrupt discontinuation of such therapy. Because beta blockade impairs the ability of the heart to respond to reflex stimuli and may increase the risks of general anesthesia and surgical procedures, resulting in protracted hypotension or low cardiac output, it has generally been suggested that such therapy should be gradually withdrawn several days prior to surgery. Recognition of the increased sensitivity to catecholamines of patients recently withdrawn from beta-blocker therapy, however, has made this recommendation controversial. If possible, beta-blockers should be withdrawn well before surgery takes place. In the event of emergency surgery, the anesthesiologist should be informed that the patient is on beta-blocker therapy
Adverse drug reactions associated with the use of beta blockers include: nausea, diarrhea, bronchospasm, dyspnea, cold extremities,

Continued...

exacerbation of Raynaud's syndrome, bradycardia, hypotension, heart failure, heart block, fatigue, dizziness, alopecia (hair loss), abnormal vision, hallucinations, insomnia, nightmares, sexual dysfunction, erectile dysfunction and/or alteration of glucose and lipid metabolism. Mixed alpha1/beta-antagonist therapy is also commonly associated with orthostatic hypotension. Carvedilol therapy is commonly associated with edema. Due to the high penetration across the blood–brain barrier, lipophilic beta blockers, such as propranolol and metoprolol, are more likely than other less lipophilic beta blockers to cause sleep disturbances, such as insomnia, vivid dreams and nightmares.
Adverse effects associated with beta2-adrenergic receptor antagonist activity (bronchospasm, peripheral vasoconstriction, alteration of glucose and lipid metabolism) are less common with beta1-selective (often termed "cardioselective") agents, but receptor selectivity diminishes at higher doses. Beta blockade, especially of the beta-1 receptor at the macula densa, inhibits renin release, thus decreasing the release of aldosterone. This causes hyponatremia and hyperkalemia.
Hypoglycemia can occur with beta blockade because beta2-adrenoceptors normally stimulate glycogen breakdown (glycogenolysis) in the liver and pancreatic release of the hormone glucagon, which work together to increase plasma glucose. Therefore, blocking beta2-adrenoceptors lowers plasma glucose. beta1-blockers have fewer metabolic side effects in diabetic patients; however, the fast heart rate that serves as a warning sign for insulin-induced low blood sugar may be masked, resulting in hypoglycemia unawareness. This is termed beta blocker-induced hypoglycemia unawareness. Therefore, beta blockers are to be used cautiously in diabetics.
Diuretics and beta blockers used for hypertension increase a patient's risk of developing diabetes mellitus.
Beta blockers must not be used in the treatment of selective alpha-adrenergic agonist overdose. The blockade of only beta receptors increases blood pressure, reduces coronary blood flow, left ventricular function, and cardiac output and tissue perfusion by means of leaving the alpha-adrenergic system stimulation unopposed.
The substance exhibits effects on the adrenergic receptors
The adverse effects seen with adrenergic drugs are broad. The most common side effects are changes in heart rate and blood pressure.
Non-selective binding to the adrenergic receptors can cause different side effects that vary based on the specific agent as well as the dosage.
The common non-selective agonists are norepinephrine, epinephrine, and isoproterenol (isoprenaline). Common side effects are tachycardia, hypertension, arrhythmias, palpitations, and anxiety. Norepinephrine is less likely to cause arrhythmias than some of the other pressor medications, probably because it is more alpha-1 receptor-selective as compared with the beta-1 receptor. [
Adrenergic receptors all have drug antagonists. Alpha-blockers are not generally indicated for the treatment of alpha-agonist overdoses.
Beta-blockers may be used to treat adverse effects arising from adrenergic receptor agonists acutely. Beta-blockers can treat tachycardia and hypertension that may occur from vasopressors. Toxicity should be monitored in the pediatric population when using beta-2 agonists as they can increase concentrations of liver aminotransferase
Many cells have these receptors, and the binding of a catecholamine to the receptor will generally stimulate the sympathetic nervous system (SNS). SNS is responsible for the fight-or-flight response, which is triggered for example by exercise or fear causing situations. This response dilates pupils, increases heart rate, mobilizes energy, and diverts blood flow from non-essential organs to skeletal muscle. These effects together tend to increase physical performance momentarily.
High catecholamine levels in blood are associated with stress, which can be induced from psychological reactions or environmental stressors such as elevated sound levels, intense light, or low blood sugar levels.
Extremely high levels of catecholamines (also known as catecholamine toxicity) can occur in central nervous system trauma due to stimulation and/or damage of nuclei in the brainstem, in particular those nuclei affecting the sympathetic nervous system. In emergency medicine, this occurrence is widely known as catecholamine dump.
Extremely high levels of catecholamine can also be caused by neuroendocrine tumours in the adrenal medulla, a treatable condition known as pheochromocytoma.
High levels of catecholamines can also be caused by monoamine oxidase A (MAO-A) deficiency. As MAO-A is one of the enzymes responsible for degradation of these neurotransmitters, its deficiency increases the bioavailability of these neurotransmitters considerably. It occurs in the absence of pheochromocytoma, neuroendocrine tumours, and carcinoid syndrome, but it looks similar to carcinoid syndrome such as facial flushing and aggression.
The acute porphyria's can cause elevated catecholamines
Epinephrine (adrenaline) reacts with both alpha- and beta-adrenoreceptors, causing vasoconstriction and vasodilation, respectively. Although alpha receptors are less sensitive to epinephrine, when activated at pharmacologic doses, they override the vasodilation mediated by beta-adrenoreceptors because there are more peripheral alpha1 receptors than beta-adrenoreceptors. The result is that high levels of circulating epinephrine cause vasoconstriction. However, the opposite is true in the coronary arteries, where beta2 response is greater than that of alpha1, resulting in overall dilation with increased sympathetic stimulation. At lower levels of circulating epinephrine (physiologic epinephrine secretion), beta-adrenoreceptor stimulation dominates since epinephrine has a higher affinity for the beta2 adrenoreceptor than the alpha1 adrenoreceptor, producing vasodilation followed by decrease of peripheral vascular resistance.
The adrenergic receptors or adrenoceptors are a class of G protein-coupled receptors that are targets of many catecholamines like norepinephrine (noradrenaline) and epinephrine (adrenaline) produced by the body, but also many medications like beta blockers,beta2 agonists and alpha2 agonists, which are used to treat high blood pressure and asthma for example.
There are two main groups of adrenoreceptors, alpha and beta, with 9 subtypes in total:
alpha types comprise the alpha1 (a Gq coupled receptor) and alpha2 (a Gi coupled receptor)[
alpha1 has 3 subtypes; alpha1A, alpha1B and alpha1D
alpha2 has 3 subtypes; alpha2A, alpha2B and alpha2C
beta types comprise the beta1, beta2 and beta3. All 3 are coupled to Gs proteins, but beta2 and beta3 also couple to Gi
Gi and Gs are linked to adenylyl cyclase. Agonist binding thus causes a rise in the intracellular concentration of the second messenger(Gi inhibits the production of cAMP) cAMP. Downstream effectors of cAMP include cAMP-dependent protein kinase (PKA), which mediates some of the intracellular events following hormone binding.
alpha-Receptors are excitatory mainly to receptors of the eye, gastrointestinal tract and vascular smooth muscle. alpha-Receptors can be further subdivided into two types. alpha-1 Receptors are primarily located in postjunctional positions and initiate postsynaptic excitatory smooth muscle and exocrine gland events. alpha-2 Receptors are primarily presynaptic inhibitors that mediate negative feedback of noradrenaline release and oppose alpha-1 stimulation. alpha-1 Receptors dominate the peripheral nervous system whilst alpha-2 receptors dominate the central nervous system. Central nervous system sympathomimetic effects result from stimulation of central adrenergic neurons. Selective agonists include phenylephrine (alpha-1,2), isoproterenol (beta-1,2), dobutamine (beta-1) and terbutaline (beta-2). Antagonists include phenoxybenzamine, a selective alpha-1 (post-synaptic) blocker and yohimbine, a selective alpha-2 (pre- synaptic) blocker.
CLINICAL EFFECTS of ADRENORECEPTOR BLOCKAGE and STIMULATION.

alpha	beta-1	beta-2
	STIMULATION	
Mydriasis Vasoconstriction Coronary dilation Decreased GI Motility Bladder contraction	Miosis Tachycardia Increased cardiac contractility Accelerated AV conduction Renin Stimulation	Miosis Vasodilation Bronchodilation Hyperglycaemia Decreased GI motility Bladder relaxation Renin release
	BLOCKADE	
Miosis Postural hypotension Reflex tachycardia Angina (uncommon) Gastric hyperacidity	Hypotension Cardiac arrhythmias Bradycardia Pulmonary oedema Hyperkalaemia	Hypoglycaemia with hypertension Bronchospasm Raynaud's phenomenon Hyperkalaemia (uncommon)

Continued...

	(uncommon) For G-protein inhibitors:/ antagonists/ modulators. G protein-coupled receptors (GPCRs) are essential cell membrane signaling molecules and represent the most important class of drug targets. Some signaling pathways downstream of a GPCR may be responsible for drug adverse effects, while others mediate therapeutic efficacy. Biased ligands preferentially activate only a subset of all GPCR signaling pathways. They hold great potential to become next-generation GPCR drugs with less side effects due to their potential to exclusively activate desired signaling pathways. GPCR ligands include odorants, tastants, and neurotransmitters, and vary in size and properties. Dramatic chemical diversity may occur even among ligands of the same receptor. Chemical variability of antagonists significantly correlates with the binding site hydrophobicity and anti-correlates with the number of hydrogen bond donors in the binding site. The number of disulfide bridges in the extracellular region of a receptor anti-correlates with the range of molecular weights of its antagonists, highlighting the role of the entrance pathway in determining the size selectivity for GPCR antagonists. The number of protein targets included in the cross-pharmacology profile of the different GPCRs changes significantly upon varying the ligand similarity and binding affinity criteria. However, with the exception of muscarinic receptors, aminergic GPCRs distinguish themselves from the rest of the members in the family by their remarkably high levels of pharmacological similarity among them. GPCRs are classified under the GRAFS system (Metabotropic Glutamate, Rhodopsin, Adhesion, Frizzled/taste2/Smoothened and Secretin), with therapies having been developed for about 30 GPCRs from the glutamate, rhodopsin and secretin families. GPCR signaling requires significant conformational changes within the trans-membrane TM domain, triggered by agonist binding, and is often coupled to interactions from the extracellular domains or loops.It is becoming clear that many binding sites and mechanisms exist for positive and negative allosteric regulation, and for biased signaling pathways, likely in greater numbers than seen in most other protein systems. When GPCRs are exposed to a neutral agonist, such as morphine on mu-opioid receptor, an occupied receptor can generate several signal waves (non-biased agonist). In GPCR signaling, the ability of a molecule to selectively activate one pathway without affecting another pathway is called biased agonism. Biased signaling occurs at different signaling proteins, including G proteins, GRKs, beta-arrestins, and even at levels of the allosteric binding site. Since GPCR activation-induced two distinct signal waves, G protein-dependent signaling followed by beta-arrestin-dependent signaling opens a new promising therapeutic future in the world of GPCRs. This is true since discovering such molecules dramatically lowers the adverse effects by turning off unwanted signals. For example, the analgesic effect of morphine (neutral agonist) through the activation of u-receptors is accompanied by several side effects, including constipation, respiratory depression, tolerance, nausea, and sedation Despite the long history and obvious desirability of developing drugs targeting GPCRs, there are several problems associated with their development. For example, the muscarinic M1 receptor is a well-validated target for agonists that could alleviate cognitive decline during neurodegeneration . Muscarinic acetylcholine receptors (MRs, or mAChRs), which are more sensitive to muscarine than to nicotine, are a group of class A GPCRs comprising five distinct subtypes, named as muscarinic M1, M2, M3, M4, and M5 receptors (M1R-M5R) M1R, M3R, and M5R are coupled to the Gq/11 family of G proteins, whereas M2R and M4R are coupled to the Gi/o family of G proteins. However, the orthosteric binding site of M1 is virtually identical to those of the related receptors M2,M3, M4, and M5 as they all bind the native ligand acetylcholine, and activation of M2 and M3 in particular gives rise to dose-limiting side effects (gastrointestinal [GI] disturbances, cardiovascular effects). Atropine and other anticholinergic agents exert their bronchodilator effects through the blockade of MRs in the airways. As a tertiary ammonium derivative, atropine is a nonselective antagonist with similar affinity for all of the MR subtypes The half-life of atropine for M3R residence is 3.5 hours. Although extensively used in the past, atropine is rarely used at the present time because it is well absorbed into the systemic circulation and penetrates the blood–brain barrier, leading to multiple systemic side effects, including tachycardia. Several long-acting muscarinic antagonists (LAMAs) are under investigation or are available for the treatment of obstructive airway diseases. LAMAs are considered to be safe drugs at recommended dosages. However, because MRs are expressed not only in the lungs, but also in the heart and the digestive and urinary tracts, the blockade of different MR subtypes in these organs by LAMA treatment can cause diverse, unwanted physiologic effects. For example, these agents can initially block prejunctional M2R on cholinergic airway nerves that normally reduce the release of the bronchoconstricting neurotransmitter acetylcholine, thus resulting in cough and paradoxical bronchoconstriction. Side effects including cardiovascular morbidity and mortality of inhaled LAMA agents in asthma need to be further studied and defined. Another potential source of side effects when targeting other receptors could arise due to signaling through multiple different pathways There are multiple signaling pathways for GPCRs, and it is sometimes possible to bias the signaling of a given GPCR through either a specific G protein or through beta arrestin which could reduce the side effects of some drugs Targeting G protein alpha-subunits has the potential for pleiotropic effects and could result in multiple side effects. Particular targets of concern include ion channels such as the G protein-activated inward rectifier K+ channel (GIRK) and the N-type voltage-gated calcium channels. Gbeta-gamma activates GIRK channels in neurons and in atria, leading to a hyperpolarization-induced decrease in action potential firing. Therefore, when considering the use of Gbeta-gamma inhibitors in cardiac or immune therapy, interfering with the regulation of action potentials would have highly undesirable side effects, such as arrhythmias. However, empirical data using prototypical Gbeta-gamma blockers indicate that these pathways are unaffected by Gbeta-gamma inhibitors, and animals treated with gallein show no signs of arrhythmias or alterations in heart rate.
CETRIMIDE & SODIUM METABISULFITE & L-ADRENALINE-D-HYDROGENTARTRATE	Asthma-like symptoms may continue for months or even years after exposure to the material ends. This may be due to a non-allergic condition known as reactive airways dysfunction syndrome (RADS) which can occur after exposure to high levels of highly irritating compound. Main criteria for diagnosing RADS include the absence of previous airways disease in a non-atopic individual, with sudden onset of persistent asthma-like symptoms within minutes to hours of a documented exposure to the irritant. Other criteria for diagnosis of RADS include a reversible airflow pattern on lung function tests, moderate to severe bronchial hyperreactivity on methacholine challenge testing, and the lack of minimal lymphocytic inflammation, without eosinophilia. RADS (or asthma) following an irritating inhalation is an infrequent disorder with rates related to the concentration of and duration of exposure to the irritating substance. On the other hand, industrial bronchitis is a disorder that occurs as a result of exposure due to high concentrations of irritating substance (often particles) and is completely reversible after exposure ceases. The disorder is characterized by difficulty breathing, cough and mucus production.

Acute Toxicity	✔	**Carcinogenicity**	✘
Skin Irritation/Corrosion	✔	**Reproductivity**	✘
Serious Eye Damage/Irritation	✔	**STOT - Single Exposure**	✘
Respiratory or Skin sensitisation	✘	**STOT - Repeated Exposure**	✘
Mutagenicity	✔	**Aspiration Hazard**	✘

Legend: ✘ *– Data either not available or does not fill the criteria for classification*
✔ *– Data available to make classification*

SECTION 12 Ecological information

Toxicity

	Endpoint	Test Duration (hr)	Species	Value	Source
Dechra Veterinary Products Tri-Solfen Topical Anaesthetic & Antiseptic Solution For Pain Relief In Lambs & Calves	Not Available	Not Available	Not Available	Not Available	Not Available

Continued...

lignocaine hydrochloride	**Endpoint**	**Test Duration (hr)**	**Species**	**Value**	**Source**
	Not Available	Not Available	Not Available	Not Available	Not Available
cetrimide	**Endpoint**	**Test Duration (hr)**	**Species**	**Value**	**Source**
	Not Available	Not Available	Not Available	Not Available	Not Available
sodium metabisulfite	**Endpoint**	**Test Duration (hr)**	**Species**	**Value**	**Source**
	EC50	72h	Algae or other aquatic plants	43.8mg/l	2
	EC50	48h	Crustacea	89mg/l	2
	EC50	96h	Algae or other aquatic plants	40mg/l	1
	LC50	96h	Fish	21mg/l	1
	NOEC(ECx)	504h	Crustacea	>10mg/l	1
bupivacaine hydrochloride	**Endpoint**	**Test Duration (hr)**	**Species**	**Value**	**Source**
	Not Available	Not Available	Not Available	Not Available	Not Available
L-adrenaline-D-hydrogentartrate	**Endpoint**	**Test Duration (hr)**	**Species**	**Value**	**Source**
	NOEC(ECx)	1h	Fish	<0.001mg/L	4
Legend:	*Extracted from 1. IUCLID Toxicity Data 2. Europe ECHA Registered Substances - Ecotoxicological Information - Aquatic Toxicity 4. US EPA, Ecotox database - Aquatic Toxicity Data 5. ECETOC Aquatic Hazard Assessment Data 6. NITE (Japan) - Bioconcentration Data 7. METI (Japan) - Bioconcentration Data 8. Vendor Data*				

Harmful to aquatic organisms, may cause long-term adverse effects in the aquatic environment.
Do NOT allow product to come in contact with surface waters or to intertidal areas below the mean high water mark. Do not contaminate water when cleaning equipment or disposing of equipment wash-waters.
Wastes resulting from use of the product must be disposed of on site or at approved waste sites.
For Bromide:
Environmental Fate: Bromide ions may be introduced to the environment after the breakdown of various salts and complexes or after the degradation of organic compounds that contain carbon bonded to bromine. Bromides may also affect the growth of micro-organisms and have been used for this purpose in industry. Bromides in drinking water are occasionally subject to disinfection processes involving ozone of chlorine. Bromide may be oxidize to produce hypobromous acid which in turn may react with natural organic matter to form brominated compounds. Bromates may also be formed following ozonation or chlorination if pH is relatively high.
Atmospheric Fate: Hydrogen bromide (HBr) and bromine nitrate (BrONO2), are much more easily broken up by sunlight causing bromine to be from 10 to 100 times more effective than chlorine at destroying ozone. From 30-60% of bromocarbons released to the atmosphere are man-made (methyl bromide fumigants and halon fire extinguishers) and both compounds are restricted by international agreement.
Ecotoxicity: Bromates may be animal carcinogens. Although not a significant toxin in mammalian or avian systems it is highly toxic to rainbow trout and Daphnia magna. On the average, sodium bromide is highly toxic to blugill, rainbow trout, sheepdhead minnow, water fleas and mysid shrimp. Bromides have a negative effect on the growth and development of oyster species.
DO NOT discharge into sewer or waterways.

Persistence and degradability

Ingredient	Persistence: Water/Soil	Persistence: Air
	No Data available for all ingredients	No Data available for all ingredients

Bioaccumulative potential

Ingredient	Bioaccumulation
	No Data available for all ingredients

Mobility in soil

Ingredient	Mobility
	No Data available for all ingredients

SECTION 13 Disposal considerations

Waste treatment methods

Product / Packaging disposal	▸ Containers may still present a chemical hazard/ danger when empty. ▸ Return to supplier for reuse/ recycling if possible. Otherwise: ▸ If container can not be cleaned sufficiently well to ensure that residuals do not remain or if the container cannot be used to store the same product, then puncture containers, to prevent re-use, and bury at an authorised landfill. ▸ Where possible retain label warnings and SDS and observe all notices pertaining to the product. 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. If it has been contaminated, it may be possible to reclaim the product by filtration, distillation or some other means. Shelf life considerations should also be

Continued...

	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 or process equipment to enter drains. ▸ It may be necessary to collect all wash water for treatment before disposal. ▸ In all cases disposal to sewer may be subject to local laws and regulations and these should be considered first. ▸ Where in doubt contact the responsible authority. ▸ Recycle wherever possible. ▸ Consult manufacturer for recycling options or consult local or regional waste management authority for disposal if no suitable treatment or disposal facility can be identified. ▸ Dispose of by: burial in a land-fill specifically licensed to accept chemical and / or pharmaceutical wastes or incineration in a licensed apparatus (after admixture with suitable combustible material). ▸ Decontaminate empty containers. Observe all label safeguards until containers are cleaned and destroyed.

SECTION 14 Transport information

Labels Required

Marine Pollutant	NO
HAZCHEM	Not Applicable

Land transport (ADG): NOT REGULATED FOR TRANSPORT OF DANGEROUS GOODS

Air transport (ICAO-IATA / DGR): NOT REGULATED FOR TRANSPORT OF DANGEROUS GOODS

Sea transport (IMDG-Code / GGVSee): NOT REGULATED FOR TRANSPORT OF DANGEROUS GOODS

14.7.1. Transport in bulk according to Annex II of MARPOL and the IBC code

Not Applicable

14.7.2. Transport in bulk in accordance with MARPOL Annex V and the IMSBC Code

Product name	Group
lignocaine hydrochloride	Not Available
cetrimide	Not Available
sodium metabisulfite	Not Available
bupivacaine hydrochloride	Not Available
L-adrenaline-D-hydrogentartrate	Not Available

14.7.3. Transport in bulk in accordance with the IGC Code

Product name	Ship Type
lignocaine hydrochloride	Not Available
cetrimide	Not Available
sodium metabisulfite	Not Available
bupivacaine hydrochloride	Not Available
L-adrenaline-D-hydrogentartrate	Not Available

SECTION 15 Regulatory information

Safety, health and environmental regulations / legislation specific for the substance or mixture

lignocaine hydrochloride is found on the following regulatory lists

Australia Chemicals with non-industrial uses removed from the Australian Inventory of Chemical Substances (old Inventory)
Australia Standard for the Uniform Scheduling of Medicines and Poisons (SUSMP) - Schedule 5

cetrimide is found on the following regulatory lists

Australia Standard for the Uniform Scheduling of Medicines and Poisons (SUSMP) - Schedule 5
Australia Standard for the Uniform Scheduling of Medicines and Poisons (SUSMP) - Schedule 6
Australian Inventory of Industrial Chemicals (AIIC)

sodium metabisulfite is found on the following regulatory lists

Australia Hazardous Chemical Information System (HCIS) - Hazardous Chemicals
Australia Standard for the Uniform Scheduling of Medicines and Poisons (SUSMP) - Schedule 5
Australian Inventory of Industrial Chemicals (AIIC)
International Agency for Research on Cancer (IARC) - Agents Classified by the IARC Monographs - Not Classified as Carcinogenic

bupivacaine hydrochloride is found on the following regulatory lists

Australia Standard for the Uniform Scheduling of Medicines and Poisons (SUSMP) - Schedule 4
Australia Standard for the Uniform Scheduling of Medicines and Poisons (SUSMP) - Schedule 5

L-adrenaline-D-hydrogentartrate is found on the following regulatory lists

Australia Standard for the Uniform Scheduling of Medicines and Poisons (SUSMP) - Schedule 3
Australia Standard for the Uniform Scheduling of Medicines and Poisons (SUSMP) - Schedule 4
Australian Inventory of Industrial Chemicals (AIIC)

Continued...

Additional Regulatory Information

Not Applicable

National Inventory Status

National Inventory	Status
Australia - AIIC / Australia Non-Industrial Use	No (bupivacaine hydrochloride)
Canada - DSL	No (cetrimide)
Canada - NDSL	No (lignocaine hydrochloride; cetrimide; sodium metabisulfite; bupivacaine hydrochloride; L-adrenaline-D-hydrogentartrate)
China - IECSC	No (cetrimide; L-adrenaline-D-hydrogentartrate)
Europe - EINEC / ELINCS / NLP	No (cetrimide)
Japan - ENCS	No (lignocaine hydrochloride; cetrimide; bupivacaine hydrochloride; L-adrenaline-D-hydrogentartrate)
Korea - KECI	No (cetrimide; bupivacaine hydrochloride; L-adrenaline-D-hydrogentartrate)
New Zealand - NZIoC	Yes
Philippines - PICCS	No (bupivacaine hydrochloride; L-adrenaline-D-hydrogentartrate)
USA - TSCA	No (cetrimide; bupivacaine hydrochloride; L-adrenaline-D-hydrogentartrate)
Taiwan - TCSI	Yes
Mexico - INSQ	No (cetrimide)
Vietnam - NCI	No (L-adrenaline-D-hydrogentartrate)
Russia - FBEPH	No (lignocaine hydrochloride; cetrimide; bupivacaine hydrochloride; L-adrenaline-D-hydrogentartrate)
Legend:	*Yes = All CAS declared ingredients are on the inventory* *No = One or more of the CAS listed ingredients are not on the inventory. These ingredients may be exempt or will require registration.*

SECTION 16 Other information

Revision Date	24/01/2022
Initial Date	12/01/2022

Other information

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.

The 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.

Definitions and abbreviations

- PC− TWA: Permissible Concentration-Time Weighted Average
- PC− STEL: Permissible Concentration-Short Term Exposure Limit
- IARC: International Agency for Research on Cancer
- ACGIH: American Conference of Governmental Industrial Hygienists
- STEL: Short Term Exposure Limit
- TEEL: Temporary Emergency Exposure Limit。
- IDLH: Immediately Dangerous to Life or Health Concentrations
- ES: Exposure Standard
- OSF: Odour Safety Factor
- NOAEL: No Observed Adverse Effect Level
- LOAEL: Lowest Observed Adverse Effect Level
- TLV: Threshold Limit Value
- LOD: Limit Of Detection
- OTV: Odour Threshold Value
- BCF: BioConcentration Factors
- BEI: Biological Exposure Index
- DNEL: Derived No-Effect Level
- PNEC: Predicted no-effect concentration

- AIIC: Australian Inventory of Industrial Chemicals
- DSL: Domestic Substances List
- NDSL: Non-Domestic Substances List
- IECSC: Inventory of Existing Chemical Substance in China
- EINECS: European INventory of Existing Commercial chemical Substances
- ELINCS: European List of Notified Chemical Substances
- NLP: No-Longer Polymers
- ENCS: Existing and New Chemical Substances Inventory
- KECI: Korea Existing Chemicals Inventory
- NZIoC: New Zealand Inventory of Chemicals
- PICCS: Philippine Inventory of Chemicals and Chemical Substances
- TSCA: Toxic Substances Control Act
- TCSI: Taiwan Chemical Substance Inventory
- INSQ: Inventario Nacional de Sustancias Químicas
- NCI: National Chemical Inventory
- FBEPH: Russian Register of Potentially Hazardous Chemical and Biological Substances

Continued...

end of SDS