Ilium Atipamezole Injection

Troy Laboratories Pty Ltd

Chemwatch Hazard Alert Code: **0**

Chemwatch: **5394-73**
Version No: **4.1**
Safety Data Sheet according to Work Health and Safety Regulations (Hazardous Chemicals) 2023 and ADG requirements

Issue Date: **23/12/2022**
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SECTION 1 Identification of the substance / mixture and of the company / undertaking

Product Identifier

Product name	Ilium Atipamezole Injection
Chemical Name	Not Applicable
Synonyms	APVMA number 66256
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	For use as a reversing agent of medetomidine in dogs and cats. To be used as directed on product label.

Details of the manufacturer or supplier of the safety data sheet

Registered company name	**Troy Laboratories Pty Ltd**
Address	37 Glendenning Road Glendenning NSW 2761 Australia
Telephone	02 8808 3600
Fax	02 9677 9300
Website	www.Troylab.com.au
Email	admin@troylab.com.au

Emergency telephone number

Association / Organisation	**Ixom Emergency Response Service**
Emergency telephone number(s)	1800 033 111 (24 hours)
Other emergency telephone number(s)	Not Available

SECTION 2 Hazards identification

Classification of the substance or mixture

Poisons Schedule	S4
Classification [1]	Non hazardous
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)	Not Applicable
Signal word	**Not Applicable**

Hazard statement(s)

Not Applicable

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Precautionary statement(s) Prevention

Not Applicable

Precautionary statement(s) Response

Not Applicable

Precautionary statement(s) Storage

Not Applicable

Precautionary statement(s) Disposal

Not Applicable

SECTION 3 Composition / information on ingredients

Substances

See section below for composition of Mixtures

Mixtures

CAS No	%[weight]	Name
104075-48-1	<1	atipamezole hydrochloride
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 eyes: ▸ Wash out immediately with water. ▸ If irritation continues, seek medical attention. ▸ 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, aerosols or combustion products are inhaled remove from contaminated area. ▸ Other measures are usually unnecessary.
Ingestion	▸ For advice, contact a Poisons Information Centre or a doctor at once. ▸ Urgent hospital treatment is likely to be needed. ▸ 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. ▸ Observe the patient carefully. ▸ Never give liquid to a person showing signs of being sleepy or with reduced awareness; i.e. becoming unconscious. ▸ Give water to rinse out mouth, then provide liquid slowly and as much as casualty can comfortably drink. ▸ Transport to hospital or doctor without delay.

Indication of any immediate medical attention and special treatment needed

Treat symptomatically.

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	None known.

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.

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	▸ **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	▸ Non combustible. ▸ Not considered a significant fire risk, however containers may burn. May emit corrosive fumes.
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. ▸ 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	▸ Avoid all personal contact, including inhalation. ▸ Wear protective clothing when risk of exposure occurs. ▸ Use in a well-ventilated area. ▸ Prevent concentration in hollows and sumps. ▸ **DO NOT** enter confined spaces until atmosphere has been checked. ▸ **DO NOT** allow material to contact humans, exposed food or food utensils. ▸ 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	▸ Polyethylene or polypropylene container. ▸ Packing as recommended by manufacturer.

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	▸ Check all containers are clearly labelled and free from leaks.
Storage incompatibility	▸ Avoid reaction with oxidising agents ▸ Avoid strong acids, bases.

SECTION 8 Exposure controls / personal protection

Control parameters

Occupational Exposure Limits (OEL)

INGREDIENT DATA

Not Available

Ingredient	Original IDLH	Revised IDLH
atipamezole hydrochloride	Not Available	Not Available

MATERIAL DATA

Exposure controls

Appropriate engineering controls

Engineering controls are used to remove a hazard or place a barrier between the worker and the hazard. Well-designed engineering controls can be highly effective in protecting workers and will typically be independent of worker interactions to provide this high level of protection.
The basic types of engineering controls are:
Process controls which involve changing the way a job activity or process is done to reduce the risk.
Enclosure and/or isolation of emission source which keeps a selected hazard "physically" away from the worker and ventilation that strategically "adds" and "removes" air in the work environment. Ventilation can remove or dilute an air contaminant if designed properly. The design of a ventilation system must match the particular process and chemical or contaminant in use. Employers may need to use multiple types of controls to prevent employee overexposure.

General exhaust is adequate under normal operating conditions. If risk of overexposure exists, wear SAA approved respirator. Correct fit is essential to obtain adequate protection. Provide adequate ventilation in warehouse or closed storage areas. Air contaminants generated in the workplace possess varying "escape" velocities which, in turn, determine the "capture velocities" of fresh circulating air required to effectively remove the contaminant.

Type of Contaminant:	Air Speed:
solvent, vapours, degreasing etc., evaporating from tank (in still air)	0.25-0.5 m/s (50-100 f/min)
aerosols, fumes from pouring operations, intermittent container filling, low speed conveyer transfers, welding, spray drift, plating acid fumes, pickling (released at low velocity into zone of active generation)	0.5-1 m/s (100-200 f/min.)
direct spray, spray painting in shallow booths, drum filling, conveyer loading, crusher dusts, gas discharge (active generation into zone of rapid air motion)	1-2.5 m/s (200-500 f/min)
grinding, abrasive blasting, tumbling, high speed wheel generated dusts (released at high initial velocity into zone of very high rapid air motion).	2.5-10 m/s (500-2000 f/min.)

Within each range the appropriate value depends on:

Lower end of the range	Upper end of the range
1: Room air currents minimal or favourable to capture	1: Disturbing room air currents
2: Contaminants of low toxicity or of nuisance value only	2: Contaminants of high toxicity
3: Intermittent, low production.	3: High production, heavy use
4: Large hood or large air mass in motion	4: Small hood - local control only

Simple theory shows that air velocity falls rapidly with distance away from the opening of a simple extraction pipe. Velocity generally decreases with the square of distance from the extraction point (in simple cases). Therefore the air speed at the extraction point should be adjusted, accordingly, after reference to distance from the contaminating source. The air velocity at the extraction fan, for example, should be a minimum of 1-2 m/s (200-400 f/min.) for extraction of solvents generated in a tank 2 meters distant from the extraction point. Other mechanical considerations, producing performance deficits within the extraction apparatus, make it essential that theoretical air velocities are multiplied by factors of 10 or more when extraction systems are installed or used.

Individual protection measures, such as personal protective equipment

Eye and face protection

- Safety glasses with side shields.
- Chemical goggles. [AS/NZS 1337.1, EN166 or national equivalent]
- 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

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	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	‣ Wear chemical protective gloves, e.g. PVC. ‣ Wear safety footwear or safety gumboots, e.g. Rubber
Body protection	See Other protection below
Other protection	‣ Overalls. ‣ P.V.C apron. ‣ Barrier cream. ‣ Skin cleansing cream. ‣ Eye wash unit.

Recommended material(s)

GLOVE SELECTION INDEX

Glove selection is based on a modified presentation of the:
"Forsberg Clothing Performance Index".
The effect(s) of the following substance(s) are taken into account in the ***computer-generated*** selection:
Ilium Atipamezole Injection

Material	CPI
BUTYL	C
NATURAL RUBBER	C
NATURAL+NEOPRENE	C
NEOPRENE	C
NITRILE	C
PVA	C
VITON	C

* CPI - Chemwatch Performance Index
A: Best Selection
B: Satisfactory; may degrade after 4 hours continuous immersion
C: Poor to Dangerous Choice for other than short term immersion
NOTE: As a series of factors will influence the actual performance of the glove, a final selection must be based on detailed observation. -
* Where the glove is to be used on a short term, casual or infrequent basis, factors such as "feel" or convenience (e.g. disposability), may dictate a choice of gloves which might otherwise be unsuitable following long-term or frequent use. A qualified practitioner should be consulted.

Ansell Glove Selection

Glove — ***In order of recommendation***
AlphaTec® 15-554
AlphaTec® Solvex® 37-185
AlphaTec® 38-612
TouchNTuff® 93-700
AlphaTec® 53-001
AlphaTec® 58-005
AlphaTec® 58-008
AlphaTec® 58-530B
AlphaTec® 58-530W
AlphaTec® 58-735

The suggested gloves for use should be confirmed with the glove supplier.

Respiratory protection

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

Selection of the Class and Type of respirator will depend upon the level of breathing zone contaminant and the chemical nature of the contaminant. Protection Factors (defined as the ratio of contaminant outside and inside the mask) may also be important.

Required minimum protection factor	Maximum gas/vapour concentration present in air p.p.m. (by volume)	Half-face Respirator	Full-Face Respirator
up to 10	1000	-AUS / Class1 P2	-
up to 50	1000	-	-AUS / Class 1 P2
up to 50	5000	Airline *	-
up to 100	5000	-	-2 P2
up to 100	10000	-	-3 P2
100+			Airline**

* - Continuous Flow ** - Continuous-flow or positive pressure demand
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)

SECTION 9 Physical and chemical properties

Information on basic physical and chemical properties

Appearance	Clear colourless liquid; mixes with water.

Physical state	Liquid	**Relative density (Water = 1)**	1.005

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Odour	Not Available	**Partition coefficient n-octanol / water**	Not Available
Odour threshold	Not Available	**Auto-ignition temperature (°C)**	Not Applicable
pH (as supplied)	4.7-5.3	**Decomposition temperature (°C)**	Not Available
Melting point / freezing point (°C)	<0	**Viscosity (cSt)**	Not Available
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)	2.37 @20C	**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
Heat of Combustion (kJ/g)	Not Available	**Ignition Distance (cm)**	Not Available
Flame Height (cm)	Not Available	**Flame Duration (s)**	Not Available
Enclosed Space Ignition Time Equivalent (s/m3)	Not Available	**Enclosed Space Ignition Deflagration Density (g/m3)**	Not Available

SECTION 10 Stability and reactivity

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

a) Acute Toxicity	Based on available data, the classification criteria are not met.
b) Skin Irritation/Corrosion	Based on available data, the classification criteria are not met.
c) Serious Eye Damage/Irritation	Based on available data, the classification criteria are not met.
d) Respiratory or Skin sensitisation	Based on available data, the classification criteria are not met.
e) Mutagenicity	Based on available data, the classification criteria are not met.
f) Carcinogenicity	Based on available data, the classification criteria are not met.
g) Reproductivity	Based on available data, the classification criteria are not met.
h) STOT - Single Exposure	Based on available data, the classification criteria are not met.
i) STOT - Repeated Exposure	Based on available data, the classification criteria are not met.
j) Aspiration Hazard	Based on available data, the classification criteria are not met.

Inhaled	The material is not thought to produce adverse health effects or irritation of the respiratory tract (as classified by EC Directives using animal models). Nevertheless, good hygiene practice requires that exposure be kept to a minimum and that suitable control measures be used in an occupational setting. Not normally a hazard due to non-volatile nature of product
Ingestion	The material has **NOT** been classified by EC Directives or other classification systems as "harmful by ingestion". This is because of the lack of corroborating animal or human evidence. The material may still be damaging to the health of the individual, following ingestion, especially where pre-existing organ (e.g liver, kidney) damage is evident. Present definitions of harmful or

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	toxic substances are generally based on doses producing mortality rather than those producing morbidity (disease, ill-health). Gastrointestinal tract discomfort may produce nausea and vomiting. In an occupational setting however, ingestion of insignificant quantities is not thought to be cause for concern.
Skin Contact	The material is not thought to produce adverse health effects or skin irritation following contact (as classified by EC Directives 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.
Eye	Although the liquid is not thought to be an irritant (as classified by EC Directives), direct contact with the eye may produce transient discomfort characterised by tearing or conjunctival redness (as with windburn).
Chronic	Long-term exposure to the product is not thought to produce chronic effects adverse to health (as classified by EC Directives using animal models); nevertheless exposure by all routes should be minimised as a matter of course.

Ilium Atipamezole Injection	**TOXICITY**	**IRRITATION**
	Not Available	Not Available
atipamezole hydrochloride	**TOXICITY**	**IRRITATION**
	Oral (Rat) LD50: 80 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***

ATIPAMEZOLE HYDROCHLORIDE	* Novartis Actions of the alpha2 adrenergic receptor agonists include:: decreased insulin release from the pancreas, increased glucagon release from the pancreas, contraction of sphincters of the GI-tract, negative feedback in the neuronal synapses - presynaptic inhibition of norepinephrine release in CNS, increased platelet aggregation (increased blood clotting tendency), decreases peripheral vascular resistance alpha2 Agonists can be used to treat: hypertension – decrease blood pressure raising actions of the sympathetic nervous system alpha2 Antagonists can be used to treat: impotence – relax penile smooth muscles and ease blood flow, depression – enhance mood by increasing norepinephrine secretion. The alpha2 receptor couples to the Gi/o protein. It is a presynaptic receptor, causing negative feedback on, for example, norepinephrine (NE). When NE is released into the synapse, it feeds back on the alpha2 receptor, causing less NE release from the presynaptic neuron. This decreases the effect of NE. There are also alpha2 receptors on the nerve terminal membrane of the post-synaptic adrenergic neuron. Adverse effects of nonselective alpha-blockers include hypotension, weakness, tachycardia, and tremulousness. Hypotension is due to inhibition of the alpha-1 receptors, which causes vascular smooth muscle relaxation and vasodilation. The remaining adverse effects occur due to the increased release of norepinephrine when alpha-2 receptors become simultaneously antagonized. This release results in the stimulation of beta receptors due to the spillover of norepinephrine and results in tremulousness and tachycardia. Adverse systemic effects such as tachycardia and tremulousness are less common with selective alpha-1 blockers. Although it can cause first-dose hypotension, syncope, dizziness, and headache due to vasodilation and vascular smooth muscle relaxation. Reflex tachycardia may occur due to a sudden decrease in blood pressure. These adverse effects tend to occur more often in the elderly and increase the risk of falls. To best avoid these adverse effects, the patient should take the medication at night. Alpha-blockers are frequently prescribed in the elderly male population, and toxicity is common in these individuals. The most common adverse effect is hypotension. Extremely low blood pressure can cause ischemic insult to major organs and increase the fall risk. If toxicity suspected, general measures are necessary to optimize the blood pressure. If a patient is hypotensive, he should be moved to a supine position until blood pressure and heart rate are acceptable. If the patient remains hypotensive, then the patient can be managed with fluid resuscitation. If necessary, vasopressors could be administered as a last resort. Preventing adverse effects of medications in the elderly population requires special care and communication between physicians, pharmacists, and nurses. Selective alpha-1 antagonists are commonly used agents in an outpatient setting for patients with benign prostatic hypertrophy. These drugs can have significant interactions with other medications that have similar adverse effects. Clinical staff Postural hypotension is particularly common after the initial dose of the alpha-1 adrenergic antagonist. Also, long term therapy has not been associated with improvement in survival; indeed at least one study has shown an increase in heart failure, stroke and cardiovascular disease with long term therapy with alpha-blockers. must review in detail the medical and social history of the patient before prescribing and ordering an alpha-blocker. Postural hypotension is particularly common after the initial dose of the alpha-1 adrenergic antagonist. Also, long term therapy has not been associated with improvement in survival; indeed at least one study has shown an increase in heart failure, stroke and cardiovascular disease with long term therapy with alpha-blockers. If a patient taking an alpha-blocker resides in a nursing facility, there should be close communication with the nursing staff closely monitoring the patient due to an increased risk of orthostatic hypotension, which can lead to a fall. Fall precautions such as bed rails, a bed alarm, and a floor protection fall mat should be a consideration. The administration of alpha-blockers requires an interprofessional team that includes physicians, pharmacists, and nurses to collaborate to prevent adverse effects, especially in the elderly. 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

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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 (uncommon)	Hypoglycaemia with hypertension Bronchospasm Raynaud's phenomenon Hyperkalaemia (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

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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.

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

Ilium Atipamezole Injection	**Endpoint**	**Test Duration (hr)**	**Species**	**Value**	**Source**
	Not Available	Not Available	Not Available	Not Available	Not Available
atipamezole hydrochloride	**Endpoint**	**Test Duration (hr)**	**Species**	**Value**	**Source**
	Not Available	Not Available	Not Available	Not Available	Not Available

Continued...

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***

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. ▸ **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. Maritime transport in bulk according to IMO instruments

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
atipamezole hydrochloride	Not Available

14.7.3. Transport in bulk in accordance with the IGC Code

Continued...

Product name	Ship Type
atipamezole hydrochloride	Not Available

SECTION 15 Regulatory information

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

atipamezole hydrochloride is found on the following regulatory lists

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

Additional Regulatory Information

Not Applicable

National Inventory Status

National Inventory	Status
Australia - AIIC / Australia Non-Industrial Use	No (atipamezole hydrochloride)
Canada - DSL	No (atipamezole hydrochloride)
Canada - NDSL	No (atipamezole hydrochloride)
China - IECSC	No (atipamezole hydrochloride)
Europe - EINEC / ELINCS / NLP	No (atipamezole hydrochloride)
Japan - ENCS	No (atipamezole hydrochloride)
Korea - KECI	No (atipamezole hydrochloride)
New Zealand - NZIoC	Yes
Philippines - PICCS	No (atipamezole hydrochloride)
USA - TSCA	No (atipamezole hydrochloride)
Taiwan - TCSI	No (atipamezole hydrochloride)
Mexico - INSQ	No (atipamezole hydrochloride)
Vietnam - NCI	No (atipamezole hydrochloride)
Russia - FBEPH	No (atipamezole hydrochloride)
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	23/12/2022
Initial Date	29/04/2020

SDS Version Summary

Version	Date of Update	Sections Updated
3.1	05/05/2020	Composition / information on ingredients - Ingredients
4.1	23/12/2022	Classification review due to GHS Revision change.

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。

Continued...

- 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
- MARPOL: International Convention for the Prevention of Pollution from Ships
- IMSBC: International Maritime Solid Bulk Cargoes Code
- IGC: International Gas Carrier Code
- IBC: International Bulk Chemical Code

- 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