

AM-251

sc-200366

Material Safety Data Sheet



The Power to Question

Hazard Alert Code Key:

EXTREME

HIGH

MODERATE

LOW

Section 1 - CHEMICAL PRODUCT AND COMPANY IDENTIFICATION

PRODUCT NAME

AM-251

STATEMENT OF HAZARDOUS NATURE

CONSIDERED A HAZARDOUS SUBSTANCE ACCORDING TO OSHA 29 CFR 1910.1200.

NFPA



SUPPLIER

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EMERGENCY

ChemWatch

Within the US & Canada: 877-715-9305

Outside the US & Canada: +800 2436 2255

(1-800-CHEMCALL) or call +613 9573 3112

SYNONYMS

C22-H21-N4-O-Cl2, "1-(2, 4-dichlorophenyl)-5-(4-iodophenyl)-4-methyl-N-1-piperidinyl-1H-", pyrazole-3-carboxamide, "AM 251", "biarylpyrazole cannabinoid receptor antagonist", "CB1 receptor antagonist/ inverse agonist"

Section 2 - HAZARDS IDENTIFICATION

CHEMWATCH HAZARD RATINGS

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

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



CANADIAN WHMIS SYMBOLS



EMERGENCY OVERVIEW

RISK

Irritating to eyes, respiratory system and skin.

POTENTIAL HEALTH EFFECTS

ACUTE HEALTH EFFECTS

SWALLOWED

■ The material has NOT been classified as "harmful by ingestion".
This is because of the lack of corroborating animal or human evidence.

EYE

■ This material can cause eye irritation and damage in some persons.

SKIN

■ This material can cause inflammation of the skin on contact in some persons.

■ The material may accentuate any pre-existing dermatitis condition.

■ Skin contact is not thought to have harmful health effects, however the material may still produce health damage following entry through wounds, lesions or abrasions.

■ Open cuts, abraded or irritated skin should not be exposed to this material.

■ Entry into the blood-stream, through, for example, cuts, abrasions or lesions, may produce systemic injury with harmful effects.

Examine the skin prior to the use of the material and ensure that any external damage is suitably protected.

INHALED

■ The material can cause respiratory irritation in some persons.

The body's response to such irritation can cause further lung damage.

■ Persons with impaired respiratory function, airway diseases and conditions such as emphysema or chronic bronchitis, may incur further disability if excessive concentrations of particulate are inhaled.

CHRONIC HEALTH EFFECTS

■ Long-term exposure to respiratory irritants may result in disease of the airways involving difficult breathing and related systemic problems. Limited evidence suggests that repeated or long-term occupational exposure may produce cumulative health effects involving organs or biochemical systems.

Long term exposure to high dust concentrations may cause changes in lung function i.e. pneumoconiosis; caused by particles less than 0.5 micron penetrating and remaining in the lung.

Section 3 - COMPOSITION / INFORMATION ON INGREDIENTS

NAME	CAS RN	%
AM251	183232-66-8	>98

Section 4 - FIRST AID MEASURES

SWALLOWED

· Immediately give a glass of water. · First aid is not generally required. If in doubt, contact a Poisons Information Center or a doctor.

EYE

■ If this product comes in contact with the eyes: · Wash out immediately with fresh running water. · Ensure complete irrigation of the eye by keeping eyelids apart and away from eye and moving the eyelids by occasionally lifting the upper and lower lids.

SKIN

■ If skin contact occurs: · Immediately remove all contaminated clothing, including footwear · Flush skin and hair with running water (and soap if available).

INHALED

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

NOTES TO PHYSICIAN

■ Treat symptomatically.

Section 5 - FIRE FIGHTING MEASURES

Vapour Pressure (mmHG):	Negligible
Upper Explosive Limit (%):	Not Available
Specific Gravity (water=1):	Not Available
Lower Explosive Limit (%):	Not Available

EXTINGUISHING MEDIA

· Foam.
· Dry chemical powder.

FIRE FIGHTING

· Alert Emergency Responders and tell them location and nature of hazard.

- Wear breathing apparatus plus protective gloves.

GENERAL FIRE HAZARDS/HAZARDOUS COMBUSTIBLE PRODUCTS

- Combustible solid which burns but propagates flame with difficulty.
 - Avoid generating dust, particularly clouds of dust in a confined or unventilated space as dusts may form an explosive mixture with air, and any source of ignition, i.e. flame or spark, will cause fire or explosion. Dust clouds generated by the fine grinding of the solid are a particular hazard; accumulations of fine dust may burn rapidly and fiercely if ignited.
- Combustion products include: carbon monoxide (CO), carbon dioxide (CO₂), hydrogen chloride, phosgene, nitrogen oxides (NO_x), other pyrolysis products typical of burning organic material.

May emit poisonous fumes.

May emit corrosive fumes.

FIRE INCOMPATIBILITY

- Avoid contamination with oxidizing agents i.e. nitrates, oxidizing acids, chlorine bleaches, pool chlorine etc. as ignition may result.

PERSONAL PROTECTION

Glasses:

Chemical goggles.

Gloves:

Respirator:

Particulate

Section 6 - ACCIDENTAL RELEASE MEASURES

MINOR SPILLS

- Clean up waste regularly and abnormal spills immediately.
- Avoid breathing dust and contact with skin and eyes.
- Wear protective clothing, gloves, safety glasses and dust respirator.
- Use dry clean up procedures and avoid generating dust.
- Vacuum up or sweep up. NOTE: Vacuum cleaner must be fitted with an exhaust micro filter (HEPA type) (consider explosion-proof machines designed to be grounded during storage and use).
- Dampen with water to prevent dusting before sweeping.
- Place in suitable containers for disposal.

MAJOR SPILLS

- Moderate hazard.

· CAUTION: Advise personnel in area.

· Alert Emergency Responders and tell them location and nature of hazard.

Section 7 - HANDLING AND STORAGE

PROCEDURE FOR HANDLING

- Avoid all personal contact, including inhalation.
 - Wear protective clothing when risk of exposure occurs.
- Empty containers may contain residual dust which has the potential to accumulate following settling. Such dusts may explode in the presence of an appropriate ignition source.
- Do NOT cut, drill, grind or weld such containers.
 - In addition ensure such activity is not performed near full, partially empty or empty containers without appropriate workplace safety authorisation or permit.

RECOMMENDED STORAGE METHODS

- Glass container.
- Polyethylene or polypropylene container.
- Check all containers are clearly labelled and free from leaks.

STORAGE REQUIREMENTS

- Store in original containers.
- Keep containers securely sealed.

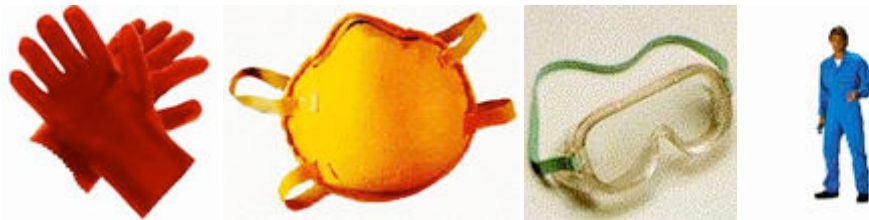
Section 8 - EXPOSURE CONTROLS / PERSONAL PROTECTION

EXPOSURE CONTROLS

The following materials had no OELs on our records

- AM251: CAS:183232-66-8

PERSONAL PROTECTION



RESPIRATOR

Particulate

Consult your EHS staff for recommendations

EYE

■ When handling very small quantities of the material eye protection may not be required.

For laboratory, larger scale or bulk handling or where regular exposure in an occupational setting occurs:

- Chemical goggles
- Face shield. Full face shield may be required for supplementary but never for primary protection of eyes
- Contact lenses may pose a special hazard; soft contact lenses may absorb and concentrate irritants. A written policy document, describing the wearing of lens or restrictions on use, should be created for each workplace or task. This should include a review of lens absorption and adsorption for the class of chemicals in use and an account of injury experience. Medical and first-aid personnel should be trained in their removal and suitable equipment should be readily available. In the event of chemical exposure, begin eye irrigation immediately and remove contact lens as soon as practicable. Lens should be removed at the first signs of eye redness or irritation - lens should be removed in a clean environment only after workers have washed hands thoroughly. [CDC NIOSH Current Intelligence Bulletin 59].

HANDS/FEET

■ Suitability and durability of glove type is dependent on usage. Important factors in the selection of gloves include: such as:

- frequency and duration of contact,
- chemical resistance of glove material,
- glove thickness and
- dexterity

Select gloves tested to a relevant standard (e.g. Europe EN 374, US F739).

- When prolonged or frequently repeated contact may occur, a glove with a protection class of 5 or higher (breakthrough time greater than 240 minutes according to EN 374) is recommended.
- When only brief contact is expected, a glove with a protection class of 3 or higher (breakthrough time greater than 60 minutes according to EN 374) is recommended.
- Contaminated gloves should be replaced.

Gloves must only be worn on clean hands. After using gloves, hands should be washed and dried thoroughly. Application of a non-perfumed moisturiser is recommended.

- Rubber gloves (nitrile or low-protein, powder-free latex). Employees allergic to latex gloves should use nitrile gloves in preference.
- Double gloving should be considered.
- PVC gloves.
- Protective shoe covers.
- Head covering.

Experience indicates that the following polymers are suitable as glove materials for protection against undissolved, dry solids, where abrasive particles are not present.

- polychloroprene
- nitrile rubber
- butyl rubber
- fluorocautchouc
- polyvinyl chloride

Gloves should be examined for wear and/ or degradation constantly.

OTHER

- For quantities up to 500 grams a laboratory coat may be suitable.
- For quantities up to 1 kilogram a disposable laboratory coat or coverall of low permeability is recommended. Coveralls should be buttoned at collar and cuffs.
- For quantities over 1 kilogram and manufacturing operations, wear disposable coverall of low permeability and disposable shoe covers.
- For manufacturing operations, air-supplied full body suits may be required for the provision of advanced respiratory protection.
- Eye wash unit.
- Ensure there is ready access to an emergency shower.
- For Emergencies: Vinyl suit.

ENGINEERING CONTROLS

■ Enclosed local exhaust ventilation is required at points of dust, fume or vapor generation.

HEPA terminated local exhaust ventilation should be considered at point of generation of dust, fumes or vapors.

Section 9 - PHYSICAL AND CHEMICAL PROPERTIES

PHYSICAL PROPERTIES

State	Divided Solid	Molecular Weight	555.24
Melting Range (°F)	Not Available	Viscosity	Not Applicable
Boiling Range (°F)	Not Applicable	Solubility in water (g/L)	Partly Miscible

Flash Point (°F)	Not Available	pH (1% solution)	Not Applicable
Decomposition Temp (°F)	Not Available	pH (as supplied)	Not Applicable
Autoignition Temp (°F)	Not Available	Vapour Pressure (mmHG)	Negligible
Upper Explosive Limit (%)	Not Available	Specific Gravity (water=1)	Not Available
Lower Explosive Limit (%)	Not Available	Relative Vapor Density (air=1)	>1
Volatile Component (%vol)	Negligible	Evaporation Rate	Not Applicable

APPEARANCE

Solid; does not mix well with water

Section 10 - CHEMICAL STABILITY

CONDITIONS CONTRIBUTING TO INSTABILITY

- Presence of incompatible materials.
- Product is considered stable.

STORAGE INCOMPATIBILITY

- Avoid reaction with oxidizing agents.

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

Section 11 - TOXICOLOGICAL INFORMATION

AM251

TOXICITY AND IRRITATION

AM251:

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

■ Asthma-like symptoms may continue for months or even years after exposure to the material ceases. This may be due to a non-allergenic condition known as reactive airways dysfunction syndrome (RADS) which can occur following exposure to high levels of highly irritating compound. Key criteria for the diagnosis of RADS include the absence of preceding respiratory disease, in a non-atopic individual, with abrupt onset of persistent asthma-like symptoms within minutes to hours of a documented exposure to the irritant. A reversible airflow pattern, on spirometry, with the presence of moderate to severe bronchial hyperreactivity on methacholine challenge testing and the lack of minimal lymphocytic inflammation, without eosinophilia, have also been included in the criteria for diagnosis of RADS. 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. Industrial bronchitis, on the other hand, is a disorder that occurs as result of exposure due to high concentrations of irritating substance (often particulate in nature) and is completely reversible after exposure ceases. The disorder is characterised by dyspnea, cough and mucus production.

CB1 selective antagonists (and inverse agonists) are used for weight reduction and smoking cessation (e.g. Rimonabant).

Considerable evidence indicates that CB1 agonists have anti-emetic effects CB1 inverse agonists do not appear to produce severe motor impairments (e.g., suppression of feeding rate or impairments in food handling) that disrupt feeding behavior. However, there is evidence that they can induce signs of nausea and malaise. CB1 neutral antagonists may decrease appetite by blocking endogenous cannabinoid tone; these drugs may be less associated with nausea than CB1 inverse agonists.

The designation of compounds as inverse agonists or neutral antagonists is based upon their signal transduction effects, which are studied at the cellular or tissue levels. Nevertheless, in behavioral pharmacology it also is important to determine if neutral antagonists block the effects of both inverse agonists and agonists at the behavioral level.

Several inverse agonists have been withdrawn from the market or from clinical trials because of concerns about neurological and psychiatric side-effects. Adverse reactions have been reported for the inverse agonist Rimonabant (an anti-obesity drug). There have been five fatal events associated with this drug. These are classified as two deaths due to cardiac disorders, one classified as "general," one as death due to infection, and one due to psychiatric disorders (suicide). Cardiac effects may have been associated with pre-existing cardiac conditions. Of the 2123 total number of adverse reactions reported, 974 were classified as psychiatric disorders, 241 were classified as nervous-system disorders, and 229 were gastrointestinal disorders. The most common psychiatric reactions were depression and related disorders of mood, of which 52 reactions involved suicidal and self-harming thoughts or behaviors. Other reported suspected adverse reactions, for rimonabant include hypoglycaemic reactions (seven reports).

The cannabinoid receptor type 1 (CB1), is a G protein-coupled cannabinoid receptor that is found in the brain and is activated by the psychoactive drug cannabis and its active compound tetrahydrocannabinol (THC) and by a group of endocannabinoid neurotransmitters including anandamide. Anandamide (AEA) was the first endogenous cannabinoid to be isolated and characterised as an agonist acting on the same receptors (CB1 and CB2) as THC.

Activation of CB1 provides neuroprotection after brain injury.

The existence of an endogenous cannabinoid system in the central nervous system and periphery has been demonstrated by research. Through a network of G-protein-coupled receptors and endogenous ligands, cannabinoids modulate several neurobiological processes including movement, cognition, and pain relief. Other research has implicated the cannabinoid system in brain development and cell migration.

Two cannabinoid receptors, CB1 and CB2, have been identified. They share high sequence homology and, not surprisingly, recognize most high-affinity agonists within the same concentration range. However selective antagonists and agonists of the two receptors have also been identified. Selective C1 agonists include analogues of endogenous N-arachidonyl ethanolamine (AEA); they bind to the CB1 receptor with very high affinity - importantly, these CB1-selective ligands retain the characteristics of CB1 receptor agonists.

Separation between the therapeutically undesirable psychotropic effects, and the clinically desirable ones however, has not been reported with agonists that bind to cannabinoid receptors. THC, as well as the two major endogenous compounds identified so far that bind to the cannabinoid receptors (anandamide and 2-arachidonylglycerol) produce most of their effects by binding to both the CB1 and CB2

cannabinoid receptors

In the liver, activation of the CB1 receptor is known to increase de novo lipogenesis. Activation of presynaptic CB1 receptors is also known to inhibit sympathetic innervation of blood vessels and contributes to the suppression of the neurogenic vasopressor response in septic shock. Inhibition of gastrointestinal activity has been observed after administration of delta9-THC, or of anandamide. This effect has been assumed to be CB1-mediated since the specific CB1 antagonist SR 141716A (Rimonabant) blocks the effect. Another report, however, suggests that inhibition of intestinal motility may also have a CB2-mediated component.

Cannabinoids are well known for their cardiovascular activity. Activation of peripheral CB1 receptors contributes to haemorrhagic and endotoxin-induced hypotension. Anandamide and 2-AG, produced by macrophages and platelets respectively, may mediate this effect.

Section 12 - ECOLOGICAL INFORMATION

No data

Section 13 - DISPOSAL CONSIDERATIONS

Disposal Instructions

All waste must be handled in accordance with local, state and federal regulations.

‡ Legislation addressing waste disposal requirements may differ by country, state and/ or territory. Each user must refer to laws operating in their area. In some areas, certain wastes must be tracked.

A Hierarchy of Controls seems to be common - the user should investigate:

- Reduction
- Reuse
- Recycling
- Disposal (if all else fails)

This material may be recycled if unused, or if it has not been contaminated so as to make it unsuitable for its intended use. Shelf life considerations should also be applied in making decisions of this type. Note that properties of a material may change in use, and recycling or reuse may not always be appropriate.

DO NOT allow wash water from cleaning equipment to enter drains. Collect all wash water for treatment before disposal.

- Recycle wherever possible.

· Consult manufacturer for recycling options or consult Waste Management Authority for disposal if no suitable treatment or disposal facility can be identified.

Section 14 - TRANSPORTATION INFORMATION

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

Section 15 - REGULATORY INFORMATION

No data for AM251 (CAS: , 183232-66-8)

Section 16 - OTHER INFORMATION

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■ Classification of the preparation and its individual components has drawn on official and authoritative sources as well as independent review by the Chemwatch Classification committee using available literature references.

A list of reference resources used to assist the committee may be found at:
www.chemwatch.net/references.

■ The (M)SDS is a Hazard Communication tool and should be used to assist in the Risk Assessment. Many factors determine whether the reported Hazards are Risks in the workplace or other settings. Risks may be determined by reference to Exposures Scenarios. Scale of use, frequency of use and current or available engineering controls must be considered.

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