

Tyrphostin AG 1478

sc-200613

Material Safety Data Sheet



The Power is Question

Hazard Alert Code Key:

EXTREME

HIGH

MODERATE

LOW

Section 1 - CHEMICAL PRODUCT AND COMPANY IDENTIFICATION

PRODUCT NAME

Tyrphostin AG 1478

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

SYNONYMS

C16-H14-Cl-N3-O2, "Tyrphostin AG-1478/ AG 1478", quinazoline, "tyrosine/ protein kinase inhibitor", "EGFR antineoplastic"

Section 2 - HAZARDS IDENTIFICATION

CHEMWATCH HAZARD RATINGS

		Min	Max
Flammability:	1		
Toxicity:	2		
Body Contact:	0		Min/Nil=0 Low=1 Moderate=2 High=3 Extreme=4
Reactivity:	0		
Chronic:	2		

CANADIAN WHMIS SYMBOLS



EMERGENCY OVERVIEW

RISK

POTENTIAL HEALTH EFFECTS

ACUTE HEALTH EFFECTS

SWALLOWED

■ Although ingestion is not thought to produce harmful effects, 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.

■ Considered an unlikely route of entry in commercial/industrial environments.

■ The most common side-effects, associated with the clinical use of Epidermal Growth Factor Receptor (EGFR) inhibitors of tyrosine kinase, in the treatment of non-small cell lung cancers (NSCLC), include diarrhoea, skin rash, nausea, vomiting, headache, dizziness, asthenia, fatigue and loss of appetite. Less common side-effects may include dryness of the mouth, skin dryness, exfoliative dermatitis, pruritus, and itchiness. Rare side-effects may include dryness of the eyes, eye pain and liver injury.

Interstitial pneumonia (sometimes fatal), may also develop as a side-effect of treatment.

High doses of some EGFR inhibitors, administered to dogs, produced decreased body weight, absence of food intake, bloody stools, tremors, emaciation, prostration, ocular changes (palpebral and bulbar conjunctiva redness, partially closed eyes, lachrymation, purulent discharge, corneal opacities, oedema, ulceration and corneal perforation), increased neutrophils and fibrinogen, cachexia, dehydration, abnormal corneal surface, and abnormal surface of the digestive tract. Microscopic findings included diffuse corneal atrophy, corneal ulcers and uveal inflammation, papillary necrosis of kidneys, inflammation and/ or haemorrhage of the digestive tract and degeneration of skeletal muscle.

EYE

■ Although the material is not thought to be an irritant, direct contact with the eye may produce transient discomfort characterized by tearing or conjunctival redness (as with windburn).

SKIN

■ The material is not thought to produce adverse health effects or skin irritation following contact (as classified using animal models). Nevertheless, good hygiene practice requires that exposure be kept to a minimum and that suitable gloves be used in an occupational setting.

INHALED

■ The material is not thought to produce adverse health effects or irritation of the respiratory tract (as classified 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.

■ 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

■ Principal routes of exposure are usually by skin contact/absorption and inhalation of generated dust.

Animal studies with some Epidermal Growth Factor Receptor (EGFR) inhibitors of tyrosine kinase, indicate that repeated doses may produce adverse effects in many tissues including the eyes.

Repeated exposures may also produce adverse effects on fertility as well as embryo- or foeto-toxicity (generally at maternally toxic levels).

Some chronic administration studies with rats have produced eosinophilic chief cells in the stomach mucosa, haematuria, hair follicular degeneration, papillary necrosis and increased ovarian atrophy, liver necrosis and mononuclear cell infiltration of the liver (in females).

In dogs, chronic studies have produced sporadic emesis, salivation, erythema, decreased absolute red blood cell counts, haematocrit and haemoglobin (in males), increased regeneration of renal proximal tubules, hair loss, ocular changes, and corneal ulceration.

The material may inhibit protein kinase. This family of kinases enzymatically catalyses the phosphorylation of protein. Because phosphorylation triggers a signaling cascade which in turn produces cell growth, inhibition effectively retards the process. There are several different inhibitors which act in this manner but most common are genistein (a naturally occurring steroid-like substance from soybeans), lavendustin (a microbial metabolite) and the tyrphostins (synthetic analogues).

Two families of protein kinase have been identified;

· serine-threonine kinases (also known as PKC) require calcium ion for their activation. The activated PKC phosphorylates proteins of the cellular signal cascade, which eventually induce expression of growth regulatory genes.

· tyrosine kinases which similarly regulate signal transmission to growth regulatory genes

Inhibition may suppress cell or tissue growth or development.

Section 3 - COMPOSITION / INFORMATION ON INGREDIENTS

NAME	CAS RN	%
4-(3-chloroanilino)-6,7-dimethoxyquinazoline	175178-82-2	>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 dust is inhaled, remove from contaminated area. · Encourage patient to blow nose to ensure clear passage of breathing. · If irritation or discomfort persists seek medical attention.

NOTES TO PHYSICIAN

- Treat symptomatically.

Section 5 - FIRE FIGHTING MEASURES

Upper Explosive Limit (%):	Not available.
Specific Gravity (water=1):	Not available
Lower Explosive Limit (%):	Not available
Relative Vapor Density (air=1):	>1

EXTINGUISHING MEDIA

- Foam.
- Dry chemical powder.

FIRE FIGHTING

- Use water delivered as a fine spray to control fire and cool adjacent area.
- DO NOT approach containers suspected to be hot.

GENERAL FIRE HAZARDS/HAZARDOUS COMBUSTIBLE PRODUCTS

- Solid which exhibits difficult combustion or is difficult to ignite.
 - 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), nitrogen oxides (NOx) and hydrogen chloride.

FIRE INCOMPATIBILITY

- Avoid contamination with strong oxidizing agents as ignition may result.

PERSONAL PROTECTION

Glasses:
Safety Glasses.
Gloves:
Respirator:
Particulate

Section 6 - ACCIDENTAL RELEASE MEASURES

MINOR SPILLS

- Clean up all spills immediately.
- Avoid contact with skin and eyes.

MAJOR SPILLS

- Clear area of personnel and move upwind.
- Alert Emergency Responders and tell them location and nature of hazard.

Section 7 - HANDLING AND STORAGE

PROCEDURE FOR HANDLING

- Limit all unnecessary personal contact.
- Wear protective clothing when risk of exposure occurs.
- Use in a well-ventilated area.
- When handling DO NOT eat, drink or smoke.
- Always wash hands with soap and water after handling.
- Avoid physical damage to containers.
- Use good occupational work practice.
- Observe manufacturer's storing and handling recommendations.

RECOMMENDED STORAGE METHODS

- Polyethylene or polypropylene container.
- Packing as recommended by manufacturer.

STORAGE REQUIREMENTS

- Keep dry.
- Store in original containers.
- Keep containers securely sealed.
- No smoking, naked lights or ignition sources.
- Store in a cool, dry, well-ventilated area.
- Store away from incompatible materials.
- Protect containers against physical damage.
- Check regularly for leaks.
- Observe manufacturer's storing and handling recommendations.

Section 8 - EXPOSURE CONTROLS / PERSONAL PROTECTION

EXPOSURE CONTROLS

Source	Material	TWA ppm	TWA mg/m³	STEL ppm	STEL mg/m³	Peak ppm	Peak mg/m³	TWA F/CC	Notes
US - Oregon Permissible Exposure Limits (Z-3)	4-(3-chloroanilino)-6,7-dimethoxyquinazoline (Inert or Nuisance Dust: Total dust)		10						(d)
US OSHA Permissible Exposure Levels (PELs) - Table Z3	4-(3-chloroanilino)-6,7-dimethoxyquinazoline (Inert or Nuisance Dust: (d) Respirable fraction)		5						
US OSHA Permissible Exposure Levels (PELs) - Table Z3	4-(3-chloroanilino)-6,7-dimethoxyquinazoline (Inert or Nuisance Dust: (d) Total dust)		15						
US - Hawaii Air Contaminant Limits	4-(3-chloroanilino)-6,7-dimethoxyquinazoline (Particulates not otherwise regulated - Total dust)		10						
US - Hawaii Air Contaminant Limits	4-(3-chloroanilino)-6,7-dimethoxyquinazoline (Particulates not otherwise regulated - Respirable fraction)		5						
US - Oregon Permissible Exposure Limits (Z-3)	4-(3-chloroanilino)-6,7-dimethoxyquinazoline (Inert or Nuisance Dust: Respirable fraction)		5						(d)
US - California Permissible Exposure Limits for Chemical Contaminants	4-(3-chloroanilino)-6,7-dimethoxyquinazoline (Particulates not otherwise regulated Respirable fraction)		5						(n)
US - Tennessee Occupational Exposure Limits - Limits For Air Contaminants	4-(3-chloroanilino)-6,7-dimethoxyquinazoline (Particulates not otherwise regulated Respirable fraction)		5						
US - Wyoming Toxic and Hazardous Substances Table Z1 Limits for Air Contaminants	4-(3-chloroanilino)-6,7-dimethoxyquinazoline (Particulates not otherwise regulated (PNOR)(f)-Respirable fraction)		5						
US - Michigan Exposure Limits for Air Contaminants	4-(3-chloroanilino)-6,7-dimethoxyquinazoline (Particulates not otherwise regulated, Respirable dust)		5						
Canada - Prince Edward Island Occupational Exposure Limits	4-(3-chloroanilino)-6,7-dimethoxyquinazoline (Particles (Insoluble or Poorly Soluble) [NOS] Inhalable particles)		10						See Appendix B current TLV/BEI Book

ENDOELTABLE

PERSONAL PROTECTION



RESPIRATOR

Particulate

Consult your EHS staff for recommendations

EYE

- Safety glasses.
- Safety glasses with side shields.

HANDS/FEET

- Wear general protective gloves, e.g.. light weight rubber gloves.

OTHER

- Overalls.
- Impervious protective clothing.
- Eyewash unit.

ENGINEERING CONTROLS

- General exhaust is adequate under normal operating conditions. If risk of overexposure exists, wear an approved respirator.

Section 9 - PHYSICAL AND CHEMICAL PROPERTIES

PHYSICAL PROPERTIES

Solid.

Does not mix with water.

State	Divided solid	Molecular Weight	315.76
Melting Range (°F)	Not available	Boiling Range (°F)	Not available
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 available		

APPEARANCE

Solid; does not mix well with water. Soluble in DMSO.

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

4-(3-CHLOROANILINO)-6,7-DIMETHOXYQUINAZOLINE

TOXICITY AND IRRITATION

4-(3-CHLOROANILINO)-6,7-DIMETHOXYQUINAZOLINE:

- No significant acute toxicological data identified in literature search.

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.

- Consult manufacturer for recycling options and recycle where possible .
- Consult Waste Management Authority for disposal.

Section 14 - TRANSPORTATION INFORMATION

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

Section 15 - REGULATORY INFORMATION

4-(3-chloroanilino)-6,7-dimethoxyquinazoline (CAS: 175178-82-2) is found on the following regulatory lists;

"US - Hawaii Air Contaminant Limits", "US - Oregon Permissible Exposure Limits (Z-3)", "US OSHA Permissible Exposure Levels (PELs) - Table Z3"

Section 16 - OTHER INFORMATION

Reasonable care has been taken in the preparation of this information, but the author makes no warranty of merchantability or any other warranty, expressed or implied, with respect to this information. The author makes no representations and assumes no liability for any direct, incidental or consequential damages resulting from its use. For additional technical information please call our toxicology department on +800 CHEMCALL.

■ 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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