

Valganciclovir Hydrochloride

sc-213141

Material Safety Data Sheet



The Power to Question

Hazard Alert Code Key:

EXTREME

HIGH

MODERATE

LOW

Section 1 - CHEMICAL PRODUCT AND COMPANY IDENTIFICATION

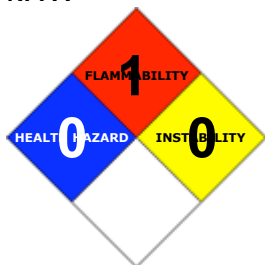
PRODUCT NAME

Valganciclovir Hydrochloride

STATEMENT OF HAZARDOUS NATURE

CONSIDERED A HAZARDOUS SUBSTANCE ACCORDING TO OSHA 29 CFR 1910.1200.

NFPA



SUPPLIER

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EMERGENCY

ChemWatch

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Outside the US & Canada: +800 2436 2255

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

SYNONYMS

C14-H22-N6-O5.HCl, "2-[(2-amino-6-oxo-3H-purin-9-yl)methoxy]-3-hydroxy-propyl] (2S)-2-", "amino-3-methyl-butanoate hydrochloride", "5-amino-3-[1-(hydroxymethyl)-2-(L-valyloxy)ethoxymethyl]-6, 7-dihydro-", "3H-imidazo[4, 5-d]pyrimidin-7-one hydrochloride", "RS 79070", RO1079070/194, "L-valine, ester with ganciclovir", Cymeval, AIDS032967, AIDS-032967, Valcyt, Valcyte, "antiviral/ viricide"

Section 2 - HAZARDS IDENTIFICATION

CHEMWATCH HAZARD RATINGS

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



CANADIAN WHMIS SYMBOLS



EMERGENCY OVERVIEW

RISK

Limited evidence of a carcinogenic effect.

POTENTIAL HEALTH EFFECTS

ACUTE HEALTH EFFECTS

SWALLOWED

- Accidental ingestion of the material may be damaging to the health of the individual.
- Adverse effects include bone-marrow suppression have been seen following use of ganciclovir.

EYE

- Although the material is not thought to be an irritant, direct contact with the eye may cause transient discomfort characterized by tearing or conjunctival redness (as with windburn).
- Slight abrasive damage may also result.

SKIN

- The material is not thought to produce adverse health effects or skin irritation following contact (as classified using animal models). Nevertheless, good hygiene practice requires that exposure be kept to a minimum and that suitable gloves be used in an occupational setting.
- 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 is not thought to produce either adverse health effects or irritation of the respiratory tract following inhalation (as classified using animal models). Nevertheless, adverse effects have been produced following exposure of animals by at least one other route and good hygiene practice requires that exposure be kept to a minimum and that suitable control measures be used in an occupational setting.
- Persons with impaired respiratory function, airway diseases and conditions such as emphysema or chronic bronchitis, may incur further disability if excessive concentrations of particulate are inhaled.
- Limited evidence exists that the substance may cause irreversible but non-lethal mutagenic effects following a single exposure.

CHRONIC HEALTH EFFECTS

- There has been concern that this material can cause cancer or mutations, but there is not enough data to make an assessment. Ample evidence from experiments exists that there is a suspicion this material directly reduces fertility. Exposure to the material may result in a possible risk of irreversible effects. The material may produce mutagenic effects in man. This concern is raised, generally, on the basis of appropriate studies with similar materials using mammalian somatic cells in vivo. Such findings are often supported by positive results from in vitro mutagenicity studies. 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. Ganciclovir was carcinogenic in the mouse at oral doses that produced exposures approximately 0.1× and 1.4×, respectively, the mean drug exposure in humans following the recommended intravenous dose of 5 mg/kg, based on area under the plasma concentration curve (AUC) comparisons. All tumours were of epithelial or vascular origin except for histiocytic sarcoma of the liver. No carcinogenic effects were seen at 1 mg/kg/day. At the higher dose there was a significant increase in the incidence of tumors of the preputial gland in males, forestomach (nonglandular mucosa) in males and females, and reproductive tissues (ovaries, uterus, mammary gland, clitoral gland and vagina) and liver in females. At the lower dose, a slightly increased incidence of tumors was noted in the preputial and harderian glands in males, forestomach in males and females, and liver in females. Ganciclovir should be considered a potential carcinogen in humans. Ganciclovir caused point mutations and chromosomal damage in mammalian cells in vitro and in vivo. In an 18 month study, ganciclovir was carcinogenic in mice after oral doses of 20 mg and 100 mg daily. Ganciclovir caused decreased mating behavior, decreased fertility, and an increased incidence of embryolethality in female mice following intravenous doses that produced an exposure approximately 1.7× the mean drug exposure in humans following the dose of 5 mg/kg, based on AUC comparisons. Ganciclovir caused decreased fertility in male mice and hypospermatogenesis in mice and dogs following daily oral or intravenous administration. Systemic drug exposure (AUC) at the lowest dose showing toxicity in each species ranged from 0.03 to 0.1× the AUC of the recommended human intravenous dose. Daily intravenous doses of 20 mg/kg did not impair female fertility but doses as low as 3 mg/kg caused reduction in the weight of pups; higher doses were associated with hypoplasia of testes and seminal vesicles in male pups. In male mice fertility was decreased after daily intravenous doses of 2 mg/kg. Effects were reversible at this dose level but became irreversible at 10 mg/kg. Valganciclovir (which metabolises to ganciclovir) caused similar effects on spermatogenesis in mice, rats, and dogs. It is considered likely that ganciclovir (and valganciclovir) could cause inhibition of human spermatogenesis. Ganciclovir has been shown to be embryotoxic in rabbits and mice following intravenous administration, and teratogenic in rabbits. Fetal resorptions were present in at least 85% of rabbits and mice administered doses that produced 2× the human exposure based on AUC comparisons. Effects observed in rabbits included: fetal growth retardation, embryolethality, teratogenicity and/or maternal toxicity. Teratogenic changes included cleft palate, anophthalmia/microphthalmia, aplastic organs (kidney and pancreas), hydrocephaly and brachygnathia. In mice, effects observed were maternal/fetal toxicity and embryolethality. Daily intravenous doses administered to female mice prior to mating, during gestation, and during lactation caused hypoplasia of the testes

and seminal vesicles in the month-old male offspring, as well as pathologic changes in the nonglandular region of the stomach. The drug exposure in mice as estimated by the AUC was approximately 1.7× the human AUC. Data obtained using an ex vivo human placental model show that ganciclovir crosses the placenta and that simple diffusion is the most likely mechanism of transfer. The transfer was not saturable over a concentration range of 1 to 10 mg/mL and occurred by passive diffusion.

Section 3 - COMPOSITION / INFORMATION ON INGREDIENTS

NAME	CAS RN	%
valganciclovir hydrochloride	175865-59-5	>98

Section 4 - FIRST AID MEASURES

SWALLOWED

· If swallowed do NOT induce vomiting. · If vomiting occurs, lean patient forward or place on left side (head-down position, if possible) to maintain open airway and prevent aspiration.

EYE

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

SKIN

■ If skin or hair contact occurs: · Flush skin and hair with running water (and soap if available). · Seek medical attention in event of irritation.

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.

for ganciclovir:

Poorly absorbed from the gastrointestinal tract. Renal excretion by glomerular filtration is the major route of elimination. Binding to plasma protein is 1-2% therefore drug interactions involving binding site displacement are not expected.

In patients who have received an overdose, dialysis and hydration may be of benefit in reducing plasma levels.

Administer activated charcoal after acute ingestion. Administer IV fluids and maintain adequate urine output. Pancytopenia and hepatitis usually improve without specific therapy. Ganciclovir can be cleared by haemodialysis but there are no reports of its use in management of overdose. Consider granulocyte colony-stimulating factor in patients with severe persistent granulocytopenia.

Valganciclovir is rapidly hydrolyses in plasma to ganciclovir which is converted to ganciclovir triphosphate by intracellular enzymes. Ganciclovir triphosphate competitively inhibits the binding of deoxyguanosine triphosphate to DNA polymerase, inhibiting DNA synthesis and terminating DNA elongation - this is the basis of viricide action.

Valganciclovir, a prodrug of ganciclovir, is well absorbed from the gastrointestinal tract and rapidly metabolized in the intestinal wall and liver to ganciclovir. The absolute bioavailability of ganciclovir from Valcyte tablets following administration with food was approximately 60% (3 studies, n=18; n=16; n=28). Ganciclovir median Tmax following administration of 450 mg to 2625 mg Valcyte tablets ranged from 1 to 3 hours. Dose proportionality with respect to ganciclovir AUC following administration of Valcyte tablets was demonstrated only under fed conditions. Systemic exposure to the prodrug, valganciclovir, is transient and low, and the AUC24 and Cmax values are approximately 1% and 3% of those of ganciclovir, respectively.

Plasma protein binding of ganciclovir is 1% to 2% over concentrations of 0.5 and 51 µg/mL. When ganciclovir was administered intravenously, the steady-state volume of distribution of ganciclovir was 0.703 ± 0.134 L/kg (n=69).

The major route of elimination of valganciclovir is by renal excretion as ganciclovir through glomerular filtration and active tubular secretion. Systemic clearance of intravenously administered ganciclovir was 3.07 ± 0.64 mL/min/kg (n=68) while renal clearance was 2.99 ± 0.67 mL/min/kg (n=16).

The terminal half-life (t½) of ganciclovir following oral administration of Valcyte tablets to either healthy or HIV-positive/CMV-positive subjects was 4.08 ± 0.76 hours (n=73), and that following administration of intravenous ganciclovir was 3.81 ± 0.71 hours (n=69). In heart, kidney, kidney-pancreas, and liver transplant patients, the terminal elimination half-life of ganciclovir following oral administration of Valcyte was 6.48 ± 1.38 hours, and following oral administration of ganciclovir capsules was 8.56 ± 3.62.

Section 5 - FIRE FIGHTING MEASURES

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

EXTINGUISHING MEDIA

· Water spray or fog.
· Foam.

FIRE FIGHTING

· Alert Emergency Responders and tell them location and nature of hazard.
· Wear breathing apparatus plus protective gloves.

GENERAL FIRE HAZARDS/HAZARDOUS COMBUSTIBLE PRODUCTS

· Combustible solid which burns but propagates flame with difficulty.

· Avoid generating dust, particularly clouds of dust in a confined or unventilated space as dusts may form an explosive mixture with air, and any source of ignition, i.e. flame or spark, will cause fire or explosion. Dust clouds generated by the fine grinding of the solid are a particular hazard; accumulations of fine dust may burn rapidly and fiercely if ignited.

Combustion products include: carbon monoxide (CO), carbon dioxide (CO₂), hydrogen chloride, phosgene, nitrogen oxides (NO_x), other pyrolysis products typical of burning organic material.

May emit poisonous 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

· valganciclovir hydrochloride: CAS:175865-59-5 CAS:175865-60-8 CAS:175865-67-5 CAS:175865-61-9 CAS:175865-62-0

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

Mixes with water.

State	Divided Solid	Molecular Weight	390.83
Melting Range (°F)	Not Available	Viscosity	Not Applicable
Boiling Range (°F)	Not Applicable	Solubility in water (g/L)	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)	Not Applicable
Volatile Component (%vol)	Negligible	Evaporation Rate	Not Applicable

APPEARANCE

White powder; does not mix well with water. The hydrochloride salt of the L-valyl ester of ganciclovir that exists as a mixture of two diastereomers. Valganciclovir HCl is a polar hydrophilic compound with a solubility of 70 mg/mL in water at 25 C at a pH of 7.0 and an n-octanol/water partition coefficient of 0.0095 at pH 7.0. The pKa for valganciclovir HCl is 7.6

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

valganciclovir hydrochloride

TOXICITY AND IRRITATION

VALGANCICLOVIR HYDROCHLORIDE:

- 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.

! Puncture containers to prevent re-use and bury at an authorized landfill.

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 valganciclovir hydrochloride (CAS: , 175865-59-5, 175865-60-8, 175865-67-5, 175865-61-9, 175865-62-0)

Section 16 - OTHER INFORMATION

Ingredients with multiple CAS Nos

Ingredient Name CAS valganciclovir hydrochloride 175865-59-5, 175865-60-8, 175865-67-5, 175865-61-9, 175865-62-0

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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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