

VALCYTE[®] Powder for Oral Solution

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

1.1. Product identifier

Product name VALCYTE[®] Powder for Oral Solution

Product code SAP-10090308

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

Use - pharmaceutical active substance (virostatic) *1

1.3. Details of the supplier of the safety data sheet

Company information

Enquiries:

Roche Products Pty Limited
Level 8, 30-34 Hickson Road
Millers Point NSW 2000
Australia

Local representation:

Phone 0061-2-9454-9624
Fax 0061-2-9971-7401
E-Mail info.sds@roche.com

1.4. Emergency telephone number

Emergency telephone number Phone 0061-2-9454-9624

*1 referring to: Valganciclovir

VALCYTE® Powder for Oral Solution

SECTION 2: Hazards identification

2.1. / 2.2. Classification of the substance or mixture / Label elements

GHS Classification

Health Hazards:

- 3.5 Germ cell mutagenicity (Category 1A)
H340 May cause genetic defects.
- 3.7 Reproductive toxicity (Category 1A)
H360FD May damage fertility. May damage the unborn child.
- 3.9 Specific target organ toxicity - Repeated exposure (Category 1)
H372 Causes damage to organs through prolonged or repeated exposure.

Signalword: Danger

Label:



Precautionary statements:

- P201 Obtain special instructions before use.
- P202 Do not handle until all safety precautions have been read and understood.
- P260 Do not breathe dust
- P281 Use personal protective equipment as required.
- P308 + P313 IF exposed or concerned: Get medical advice/attention.

Australian Remark

- HAZARDOUS SUBSTANCE. NON-DANGEROUS GOODS.
- Poisons Schedule - Schedule 4 ^{*1}
- Listed on the Australian Inventory of Chemical Substances (AICS) ^{*2}
- Listed on the Australian Inventory of Chemical Substances (AICS) ^{*3}
- Listed on the Australian Inventory of Chemical Substances (AICS) ^{*4}
- Listed on the Australian Inventory of Chemical Substances (AICS) ^{*5}

2.3. Other hazards

Note

- no information available

- *1 referring to: Valganciclovir
- *2 referring to: Mannitol
- *3 referring to: Fumaric acid
- *4 referring to: Povidone K30
- *5 referring to: Sodium benzoate

SECTION 3: Composition/information on ingredients

Characterization

consisting of 46% Valganciclovir hydrochloride, with the remainder consisting of excipients that are not classified as hazardous

Synonyms

- VALCYTE Powder for Oral Solution 50 mg/ml
- VALCYTE Dry Syrup 250 mg/5 ml

VALCYTE® Powder for Oral Solution

Ingredient	Concentration	GHS-Classification (pure ingredient)
Valganciclovir hydrochloride 175865-59-5	45.9 %	- Germ cell mutagenicity (Category 1A), H340 - Reproductive toxicity (Category 1A), H360FD - Specific target organ toxicity - Repeated exposure (Category 1), H372
Mannitol 69-65-8	48.2 %	
Fumaric acid 110-17-8	1.7 %	
Povidone K30 9003-39-8	1.7 %	
Sodium benzoate 532-32-1	0.8 %	

For the full text of the 'Hazard statements' mentioned in this Section, see Section 16.

SECTION 4: First aid measures

4.1. Description of first aid measures

Eye contact	- rinse immediately with tap water for at least 20 minutes - open eyelids forcibly - begin with medical treatment.
Skin contact	- remove immediately contaminated clothes, wash affected skin with water and soap - do not use any solvents
Inhalation	- remove the casualty to fresh air and keep him/her calm - get medical treatment
Ingestion	- summon a physician immediately

4.2. Most important symptoms and effects, both acute and delayed

Note	- no information available
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4.3. Indication of any immediate medical attention and special treatment needed

Note to physician	- treat symptomatically - preserve blood and urine samples
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SECTION 5: Firefighting measures

5.1. Extinguishing media

Suitable extinguishing media	- water spray jet, dry powder, foam, carbon dioxide, adapt extinguishing media to surrounding fire conditions
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VALCYTE® Powder for Oral Solution

Unsuitable extinguishing media - full water jet

5.2. Special hazards arising from the substance or mixture

Specific hazards - formation of toxic and corrosive combustion gases (ammonia, hydrogen chloride, nitrogen oxides) possible

5.3. Advice for firefighters

Protection of fire-fighters - precipitate gases/vapours/mists with water spray
- chemical incident emergency response unit with full protective equipment

SECTION 6: Accidental release measures

6.1. Personal precautions, protective equipment and emergency procedures

Personal precautions - prevent any exposure

6.2. Environmental precautions

Environmental protection - do not allow to enter drains or waterways

6.3. Methods and material for containment and cleaning up

Methods for cleaning up - collect solids (avoid dust formation) and hand over to waste removal
- clean contaminated areas with little ethanol

SECTION 7: Handling and storage

7.1. Precautions for safe handling

Suitable materials - aluminium, glass, stainless steel, enamel, polyethylene

7.2. Conditions for safe storage, including any incompatibilities

Storage conditions - below 30 °C
- in closed containers
- protected from light

Validity - see "best use before" date stated on the label
- 36 months, ≤ 30 °C, see "best use before" date stated on the label

Packaging materials - amber glass bottles with child resistant plastic closure
- polyethylene bag in metal drum

SECTION 8: Exposure controls/personal protection

8.1. Control parameters

Threshold value (Roche) air - IOEL (Internal Occupational Exposure Limit): 0.008 mg/m³ *1

8.2. Exposure controls

- General protective and hygiene measures - instruction of employees mandatory
 - cleanse skin thoroughly after work, apply skin cream
- Respiratory protection - in case of open handling or accidental release:
 particle mask or respirator with independent air supply
- Hand protection - protective gloves (eg made of neoprene, nitrile or butyl rubber)
- Eye protection - safety glasses

*1 referring to: Valganciclovir

SECTION 9: Physical and chemical properties

9.1. Information on basic physical and chemical properties

Colour white to slightly yellow

Form granules

Solubility 10'370 mg/l, ethanol 95 % *1
 ~ 30 mg/l, acetone *1
 ~ 2'990 mg/l, hexane *1
 ~ 70'000 mg/l, water *1

Partition coefficient log P_{ow} 0.009 (n-octanol/buffer°C) pH 6.9 *1

Melting temperature 175 °C (with decomposition) *1

9.2. Other information

Dissociation constant pK₁ 7.6 *1

Solubility properties

Hydrolysis hydrolytically unstable, in alkaline solution *1

*1 referring to: Valganciclovir

SECTION 10: Stability and reactivity

10.1. Reactivity

Note - no information available

10.2. Chemical stability

Note - no information available

10.3. Possibility of hazardous reactions

Note - no information available

10.4. Conditions to avoid

Conditions to avoid - warming
- humidity

10.5. Incompatible materials

Materials to avoid - strong oxidizing agents *1

10.6. Hazardous decomposition products

Note - tends to racemise and hydrolyse quickly in neutral and basic aqueous solution *1

*1 referring to: Valganciclovir

SECTION 11: Toxicological information

11.1. Information on toxicological effects

Acute toxicity - LD₅₀ > 2'000 mg/kg (oral, mouse) *1

Chronic toxicity - NOAEL 2 mg/kg/d (oral, rat; 90 days) *1

Local effects - skin: non-irritant (rabbit) *1

Sensitization - non-sensitizing (guinea pig) *1

Mutagenicity - mutagenic *1

Carcinogenicity - carcinogenic *6

Reproductive toxicity - teratogenic and embryotoxic *6
- may lower parental fertility *6

STOT-single exposure - no information available

VALCYTE® Powder for Oral Solution

STOT-repeated exposure	- no information available	
Aspiration hazard	- no information available	
Note	- causes testicular atrophy as well as renal and hematologic changes	*1
*1 referring to:	Valganciclovir	
*6 referring to:	Ganciclovir	

SECTION 12: Ecological information

12.1. Toxicity

Ecotoxicity	- barely toxic for planktonic crustaceans (<i>Daphnia magna</i>) EC ₅₀ (48 h) > 1010 mg/l (average measured concentration) NOEC (48 h) 1010 mg/l (average measured concentration)	*6
	- barely toxic for fish (rainbow trout) LC ₅₀ (96 h) > 1020 mg/l (average measured concentration) NOEC (96 h) 1020 mg/l (average measured concentration)	*6
	- barely toxic for fish (bluegill sunfish) LC ₅₀ (96 h) > 1020 mg/l (average measured concentration) NOEC (96 h) 1020 mg/l (average measured concentration)	*6
	- barely toxic for bluegreen algae (nominal concentration > 100 mg/l) (<i>Nostoc</i> sp.) NOEC (12 d) 1000 mg/l (FDA Technical Assistance Document No. 4.02)	*6
	- barely toxic for microorganisms (bacteria, fungi, cyanobacteria in pure culture) NOEC 1000 mg/l	*6

12.2. Persistence and degradability

Inherent biodegradability	- not inherently biodegradable 2 %, 28 days	*6
	- evidence for medium-term biodegradation in surface waters 34 %, 28 d (analogous to OECD 308, Transformation in natural water/sediment systems)	*6

12.3. Bioaccumulative potential

Note	- no information available	
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12.4. Mobility in soil

Mobility	- barely volatile (water-air) K _H = 0.00000026 Pa·m ³ /mol (vapour pressure/water solubility)	*6
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12.5. Results of PBT and vPvB assessment

Note	- no information available	
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VALCYTE® Powder for Oral Solution

12.6. Other adverse effects

Note - no information available

*6 referring to: Ganciclovir

SECTION 13: Disposal considerations

13.1. Waste treatment methods

Waste from residues

- incinerate in qualified installation with flue gas scrubbing
- observe local/national regulations regarding waste disposal
- return to supplier or hand over to authorised disposal company
- medicines should not be disposed of via wastewater

SECTION 14: Transport information

Australian Remark - ADG Code: This product is not classified as a dangerous good. No special transport conditions are necessary unless required by other regulations.

SECTION 15: Regulatory information

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

Water hazard class (Germany) 3: strongly hazardous for water (according to annex 4 of directive VwVwS of 17.05.1999)

Regulatory status (Australia) - This product has been approved by the Therapeutic Goods Administration (TGA); AUST R 154382

SECTION 16: Other information

Safety-lab number - BS-6697 *1

Full text of H-Statements referred to under section 3

H340 May cause genetic defects.
H360FD May damage fertility. May damage the unborn child.
H372 Causes damage to organs through prolonged or repeated exposure.

Note - Valganciclovir is a valyl ester prodrug of ganciclovir, which after oral administration is rapidly and extensively converted to ganciclovir during the absorption process *1

Edition documentation - changes from previous version in sections 2

*1 referring to: Valganciclovir

The information in this safety data sheet is based on current scientific knowledge. It should not be taken as expressing or implying any warranty concerning product characteristics.

SECTION 1: Identification of the substance/mixture and of the company/undertaking**1.1. Product identifier**

Product name VALCYTE® F.C. Tablets 450 mg

Product code SAP-10069575

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

Use - pharmaceutical active substance (virostatic) *1

1.3. Details of the supplier of the safety data sheet

Company information

Enquiries:

Roche Products Pty Limited

P.O. Box 255

Dee Why, N.S.W. 2099

AUS-Australia

Australia

Local representation:

Phone 0061-2-9454-9624

Fax 0061-2-9971-7401

E-Mail info.sds@roche.com

1.4. Emergency telephone number

Emergency telephone number Phone 0061-2-9454-9624

*1 referring to: Valganciclovir

SECTION 2: Hazards identification

2.1. / 2.2. Classification of the substance or mixture / Label elements

GHS Classification

Health Hazards:

- 3.5 Germ cell mutagenicity (Category 1A)
H340 May cause genetic defects.
- 3.7 Reproductive toxicity (Category 1A)
H360FD May damage fertility. May damage the unborn child.
- 3.9 Specific target organ toxicity - Repeated exposure (Category 1)
H372 Causes damage to organs through prolonged or repeated exposure.

Signalword: Danger

Label:



Precautionary statements:

- P201 Obtain special instructions before use.
- P202 Do not handle until all safety precautions have been read and understood.
- P260 Do not breathe dust
- P281 Use personal protective equipment as required.
- P308 + P313 IF exposed or concerned: Get medical advice/attention.

Australian Remark

- HAZARDOUS SUBSTANCE. NON-DANGEROUS GOODS.
- Poisons Schedule - Schedule 4 *1
- Listed on the Australian Inventory of Chemical Substances (AICS) *2
- Listed on the Australian Inventory of Chemical Substances (AICS) *3

2.3. Other hazards

Note

- no information available

*1 referring to: Valganciclovir

*2 referring to: Cellulose

*3 referring to: Crospovidone

SECTION 3: Composition/information on ingredients

Characterization

consisting of 81% Valganciclovir hydrochloride, with the remainder consisting of excipients that are not classified as hazardous

VALCYTE® F.C. Tablets 450 mg

Ingredient	Concentration	GHS-Classification (pure ingredient)
Valganciclovir hydrochloride 175865-59-5	81 %	- Germ cell mutagenicity (Category 1A), H340 - Reproductive toxicity (Category 1A), H360FD - Specific target organ toxicity - Repeated exposure (Category 1), H372
Microcrystalline cellulose 9004-34-6		
Crospovidone 9003-39-8		

For the full text of the 'Hazard statements' mentioned in this Section, see Section 16.

SECTION 4: First aid measures

4.1. Description of first aid measures

Eye contact	- rinse immediately with tap water for at least 20 minutes - open eyelids forcibly
Skin contact	- remove immediately contaminated clothes, wash affected skin with water and soap - do not use any solvents
Inhalation	- remove the casualty to fresh air and keep him/her calm - in the event of symptoms get medical treatment
Ingestion	- summon a physician immediately

4.2. Most important symptoms and effects, both acute and delayed

Note	- no information available
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4.3. Indication of any immediate medical attention and special treatment needed

Note to physician	- treat symptomatically - preserve blood and urine samples
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SECTION 5: Firefighting measures

5.1. Extinguishing media

Suitable extinguishing media	- water spray jet, dry powder, foam, carbon dioxide, adapt extinguishing media to surrounding fire conditions
Unsuitable extinguishing media	- full water jet

5.2. Special hazards arising from the substance or mixture

Specific hazards	- formation of toxic and corrosive combustion gases (ammonia, hydrogen chloride, nitrogen oxides) possible
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VALCYTE® F.C. Tablets 450 mg

5.3. Advice for firefighters

- Protection of fire-fighters
- precipitate gases/vapours/mists with water spray
 - chemical incident emergency response unit with full protective equipment

SECTION 6: Accidental release measures

6.1. Personal precautions, protective equipment and emergency procedures

- Personal precautions
- prevent any exposure

6.2. Environmental precautions

- Environmental protection
- do not allow to enter drains or waterways

6.3. Methods and material for containment and cleaning up

- Methods for cleaning up
- collect solids (avoid dust formation) and hand over to waste removal
 - clean contaminated areas with little ethanol

SECTION 7: Handling and storage

7.1. Precautions for safe handling

- Suitable materials
- aluminium, glass, stainless steel, enamel, polyethylene

7.2. Conditions for safe storage, including any incompatibilities

- Storage conditions
- below 30 °C
 - in closed containers
 - protected from light
- Validity
- 36 months, ≤ 30 °C, see "best use before" date stated on the label
- Packaging materials
- high density polyethylene (HDPE) bottles with a child-resistant polypropylene screw cap

SECTION 8: Exposure controls/personal protection

8.1. Control parameters

- Threshold value (Roche) air
- IOEL (Internal Occupational Exposure Limit): 0.008 mg/m³ *1

VALCYTE® F.C. Tablets 450 mg

8.2. Exposure controls

General protective and hygiene measures	- instruction of employees mandatory - cleanse skin thoroughly after work, apply skin cream
Respiratory protection	- in case of open handling or accidental release: particle mask or respirator with independent air supply
Hand protection	- protective gloves (eg made of neoprene, nitrile or butyl rubber)
Eye protection	- safety glasses

*1 referring to: Valganciclovir

SECTION 9: Physical and chemical properties

9.1. Information on basic physical and chemical properties

Colour	pink pale red	
Form	oval, biconvex tablet	
Solubility	10'370 mg/l, ethanol 95 % ~ 30 mg/l, acetone ~ 2'990 mg/l, hexane ~ 70'000 mg/l, water	*1 *1 *1 *1
Partition coefficient	log P _{ow} 0.009 (n-octanol/buffer°C) pH 6.9	*1
Melting temperature	175 °C (with decomposition)	*1

9.2. Other information

Dissociation constant	pK ₁ 7.6	*1
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Solubility properties

Hydrolysis	hydrolytically unstable, in alkaline solution	*1
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*1 referring to: Valganciclovir

SECTION 10: Stability and reactivity

10.1. Reactivity

Note	- no information available
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10.2. Chemical stability

Note	- no information available
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VALCYTE® F.C. Tablets 450 mg

10.3. Possibility of hazardous reactions

Note - no information available

10.4. Conditions to avoid

Conditions to avoid - warming
- humidity

10.5. Incompatible materials

Materials to avoid - strong oxidizing agents *1

10.6. Hazardous decomposition products

Note - tends to racemise and hydrolyse quickly in neutral and basic aqueous solution *1

*1 referring to: Valganciclovir

SECTION 11: Toxicological information

11.1. Information on toxicological effects

Acute toxicity - LD₅₀ > 2'000 mg/kg (oral, mouse) *1

Chronic toxicity - NOAEL 2 mg/kg/d (oral, rat; 90 days) *1

Local effects - skin: non-irritant (rabbit) *1

Sensitization - non-sensitizing (guinea pig) *1

Mutagenicity - mutagenic *1

Carcinogenicity - carcinogenic *4

Reproductive toxicity - teratogenic and embryotoxic *4
- may lower parental fertility *4

STOT-single exposure - no information available

STOT-repeated exposure - no information available

Aspiration hazard - no information available

Note - causes testicular atrophy as well as renal and hematologic changes *1

*1 referring to: Valganciclovir

*4 referring to: Ganciclovir

SECTION 12: Ecological information

12.1. Toxicity

Ecotoxicity	<ul style="list-style-type: none"> - barely toxic for planktonic crustaceans (Daphnia magna) EC₅₀ (48 h) > 1010 mg/l (average measured concentration) NOEC (48 h) 1010 mg/l (average measured concentration) *4 - barely toxic for fish (rainbow trout) LC₅₀ (96 h) > 1020 mg/l (average measured concentration) NOEC (96 h) 1020 mg/l (average measured concentration) *4 - barely toxic for fish (bluegill sunfish) LC₅₀ (96 h) > 1020 mg/l (average measured concentration) NOEC (96 h) 1020 mg/l (average measured concentration) *4 - barely toxic for bluegreen algae (nominal concentration > 100 mg/l) (Nostoc sp.) NOEC (12 d) 1000 mg/l (FDA Technical Assistance Document No. 4.02) *4 - barely toxic for microorganisms (bacteria, fungi, cyanobacteria in pure culture) NOEC 1000 mg/l *4
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12.2. Persistence and degradability

Inherent biodegradability	<ul style="list-style-type: none"> - not inherently biodegradable 2 %, 28 days *4 - evidence for medium-term biodegradation in surface waters 34 %, 28 d (analogous to OECD 308, Transformation in natural water/sediment systems) *4
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12.3. Bioaccumulative potential

Note - no information available

12.4. Mobility in soil

Mobility	<ul style="list-style-type: none"> - barely volatile (water-air) K_H = 0.00000026 Pa*m³/mol (vapour pressure/water solubility) *4
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12.5. Results of PBT and vPvB assessment

Note - no information available

12.6. Other adverse effects

Note - no information available

*4 referring to: Ganciclovir

VALCYTE® F.C. Tablets 450 mg

SECTION 13: Disposal considerations

13.1. Waste treatment methods

- Waste from residues
- return to supplier or hand over to authorised disposal company
 - observe local/national regulations regarding waste disposal
 - incinerate in qualified installation with flue gas scrubbing
 - medicines should not be disposed of via wastewater

SECTION 14: Transport information

- Australian Remark
- ADG Code: This product is not classified as a dangerous good. No special transport conditions are necessary unless required by other regulations.

SECTION 15: Regulatory information

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

Water hazard class (Germany) 3: strongly hazardous for water (according to annex 4 of directive VwVwS of 17.05.1999)

- Regulatory status (Australia)
- This product has been approved by the Therapeutic Goods Administration (TGA); AUST R 82906

SECTION 16: Other information

Safety-lab number - BS-6697 *1

Full text of H-Statements referred to under section 3

- H340 May cause genetic defects.
H360FD May damage fertility. May damage the unborn child.
H372 Causes damage to organs through prolonged or repeated exposure.

- Note
- Valganciclovir is a valyl ester prodrug of ganciclovir, which after oral administration is rapidly and extensively converted to ganciclovir during the absorption process *1
 - 496.3 mg Valganciclovir hydrochloride per tablet is equivalent to 450 mg free base

Edition documentation - changes from previous version in sections 1, 2, 3

*1 referring to: Valganciclovir

The information in this safety data sheet is based on current scientific knowledge. It should not be taken as expressing or implying any warranty concerning product characteristics.