

Safety Data Sheet

Vemurafenib pure

according to Regulation (EU) nr. 1907/2006

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

1.1. Product identifier

Product name Vemurafenib pure
Product code SAP-12049465

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

Use - pharmaceutical active substance (antineoplastic)

1.3. Details of the supplier of the safety data sheet

Company information	Enquiries: F. Hoffmann-La Roche AG Postfach CH-4070 Basel Switzerland	Local representation:
	Phone +41-61/688 54 80	
	Fax +41-61/681 72 76	
	E-Mail info.sds@roche.com	

1.4. Emergency telephone number

Emergency telephone number Phone +41-61/688 54 80

SECTION 2: Hazards identification

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

GHS Classification Environmental Hazards:
4.1 Hazardous to the aquatic environment (Category 1)
H410 Very toxic to aquatic life with long lasting effects.

Signalword: Warning

Label:



Precautionary statements:

- P273 Avoid release to the environment.
- P312 Call a POISON CENTER or doctor/physician if you feel unwell.

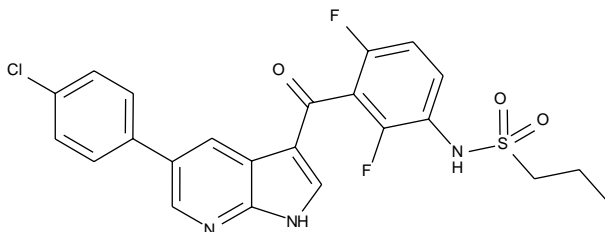
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2.3. Other hazards

Note - no further information available

SECTION 3: Composition/information on ingredients

Chemical name	- N-[3-[[5-(4-chlorophenyl)-1H-pyrrolo[2,3-b]pyridin-3-yl]carbonyl]-2,4-difluorophenyl]-1-propanesulfonamide
Synonyms	- SAC04 - SAC-RO5185426-000 pure
CAS number	918504-65-1
UN number	3077
Roche number	RO5185426-000
Empirical formula	C ₂₃ H ₁₈ ClF ₂ N ₃ O ₃ S
Molecular mass	489.93 g/mol



SECTION 4: First aid measures

4.1. Description of first aid measures

Eye contact	- rinse immediately with tap water for 10 minutes - open eyelids forcibly - consult a physician if irritation persists
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

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

Note - no information available

4.3. Indication of any immediate medical attention and special treatment needed

Note to physician - treat symptomatically

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

5.2. Special hazards arising from the substance or mixture

- Specific hazards
- very high probability of ignition of dust whirled up
 - severe dust explosion hazard
 - formation of toxic and corrosive combustion gases (hydrogen chloride, hydrogen fluoride, nitrogen oxides) possible
 - substance is hazardous for water: contain fire-fighting wastewater

5.3. Advice for firefighters

- Protection of fire-fighters
- precipitate gases/vapours/mists with water spray
- Special method of fire-fighting
- cool endangered containers with water spray

SECTION 6: Accidental release measures

6.1. Personal precautions, protective equipment and emergency procedures

- Personal precautions
- ensure adequate ventilation

6.2. Environmental precautions

- Environmental protection
- do not allow to enter drains or waterways
 - if the substance reaches waters or the sewer system, inform the competent authority

6.3. Methods and material for containment and cleaning up

- Methods for cleaning up
- collect spilled material (avoid dust formation) and hand over to waste removal in sealed containers

SECTION 7: Handling and storage

7.1. Precautions for safe handling

- Technical measures
- processing in closed systems, if possible superposed by inert gas (e.g. nitrogen)
 - avoid dust formation; high dust explosion hazard
 - high probability of ignition: ground plant, avoid effective ignition sources; avoid electrostatic charging of dust clouds

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7.2. Conditions for safe storage, including any incompatibilities

Storage conditions	- room temperature - protected from light and humidity
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SECTION 8: Exposure controls/personal protection

8.1. Control parameters

Threshold value (Roche) air	- IOEL (Internal Occupational Exposure Limit): 0.015 mg/m ³
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8.2. Exposure controls

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
Body protection	- wear conductive shoes

SECTION 9: Physical and chemical properties

9.1. Information on basic physical and chemical properties

Colour	white to slightly yellow
Form	powder
Solubility	0.00271 mg/l, water (20 °C, pH 8, OECD No. 105) ≤ 6.1 mg/l, aquatic ecotoxicity media (25 °C, HPLC) soluble, tetrahydrofuran
Partition coefficient	log P _{ow} 4.74 pH 5 log P _{ow} 3.80 pH 7 log P _{ow} 3.26 pH 9 (HPLC Method, OECD No. 117)
Melting temperature	272 °C

9.2. Other information

Dissociation constant	pK ₁ 7.9 pK ₂ 11.1 (25 °C, acidic group(s), titrimetric determination)
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SECTION 10: Stability and reactivity

10.1. Reactivity

Note - no information available

10.2. Chemical stability

Stability - stable under normal conditions

10.3. Possibility of hazardous reactions

Note - no information available

10.4. Conditions to avoid

Conditions to avoid

- humidity
- light
- warming

10.5. Incompatible materials

Note - no information available

10.6. Hazardous decomposition products

Note - no information available

SECTION 11: Toxicological information

11.1. Information on toxicological effects

Acute toxicity	- NOEL 1'000 mg/kg (oral, rat)
Subacute toxicity	- NOAEL 1'000 mg/kg/d (oral, rat, 28 d)
Local effects	- skin: non-irritant (rabbit; OECD No. 404) - phototoxic (in vitro)
Sensitization	- not skin sensitizing (guinea pig) (OECD No. 406)
Subchronic toxicity	- NOAEL 450 mg/kg/d (oral, rat; 13 weeks)
Mutagenicity	- not mutagenic (Ames test; OECD No. 471 (Salmonella typhimurium)) - does not induce chromosomal aberrations in vitro (various in vitro test systems)
Reproductive toxicity	- not teratogenic (oral, rat) - not teratogenic (oral, rabbit); NOAEL = 450 mg/kg/d

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- not embryotoxic (150 mg/kg/d; oral, rabbit, female, 14 d); NOAEL = 150 mg/kg/d

SECTION 12: Ecological information

12.1. Toxicity

Ecotoxicity

- strongly toxic for algae (*Pseudokirchneriella subcapitata*)
ErC₅₀ (72 h) 21.91 mg/l (nominal concentration)
ErC₅₀ (72 h) 2.832 mg/l (average measured concentration)
NOEC (72 h) 0.156 mg/l (average measured concentration)
(OECD No. 201)
- barely toxic for planktonic crustaceans (nominal concentration = 100 mg/l) (*Daphnia magna*)
EC₅₀ (48 h) > 100 mg/l (nominal concentration)
NOEC (48 h) 0.27 mg/l
(OECD No. 202)
- barely toxic for fish (nominal concentration = 100 mg/l) (guppy)
LC₅₀ (96 h) > 100 mg/l (nominal concentration)
NOEC (96 h) ≥ 0.27 mg/l
(OECD No. 203)
- daphnid reproduction test (*Daphnia magna*)
NOEC (21 d) 0.0171 mg/l (average measured concentration)
(OECD No. 211)
- fish early life stage test (zebrafish)
NOEC (35 d) 1.63 mg/l (average measured concentration)
(OECD No. 210)
- barely inhibitory on aerobic bacterial respiration (activated sludge)
NOEC (3 h) 301 mg/l (nominal concentration)
(OECD No. 209)

12.2. Persistence and degradability

Inherent biodegradability

- not inherently biodegradable
< 10 %, 28 d
(MITI Test II, OECD No. 302 C)

Environmental fate

- very persistent in a sediment/water fate test, no transformation products identified
(OECD 308, Transformation in natural water/sediment systems)

12.3. Bioaccumulative potential

Bioconcentration

- slightly accumulating, relatively high depuration rate (zebrafish)
Bioaccumulation factor:
BCF 62.2 to 85.1, 28 d
BCF_k 62.0 to 133.9, 28 d
Depuration:
DT₅₀ ≤ 0.6 d
DT₉₀ ≤ 2 d
(Bioconcentration: flow-through fish test; OECD no. 305)

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12.4. Mobility in soil

Mobility

- strong adsorption, immobile (, 25 °C)
- $K_{oc} = 3739$ to 55454 l/kg (soil, activated sludge)
- $K_d = 1492$ l/kg (soil)
- $K_d = 6022$ l/kg (activated sludge)
- (OECD No. 106 Adsorption/Desorption)

12.5. Results of PBT and vPvB assessment

PBT/vPvB

- not PBT, not vPvB

12.6. Other adverse effects

Note

- no information available

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

SECTION 14: Transport information

IATA	Class	UN/ID	PG		PI	Label	Mark	
	9	3077	III		956/956	9	EHS	
IMDG	Class	UN	PG	EmS	PI	Label	Mark	
	9	3077	III	F-A S-F	P002/IBC08	9	marine pollutant	
RID/ADR	Class	UN	PG	Haz.no	PI	Label	Mark	Classif. code
	9	3077	III	90	P002/IBC08	9	EHS	M7

Proper shipping name

ENVIRONMENTALLY HAZARDOUS SUBSTANCE, SOLID, N.O.S.

Technical name

Vemurafenib

SECTION 15: Regulatory information

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

Water hazard class (Germany)	2: hazardous for water (own classification according to directive VwVwS of 27.07.2005)
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SECTION 16: Other information

Safety-lab number	- BS-9076 - BS-9274 - BS-9349
Edition documentation	- changes from previous version in sections 2

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.