Safety Data Sheet

Cobimetinib

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	Cobimetinib
Product code	SAP-12052714

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 Phone +41-61/688 54 80 Fax +41-61/681 72 76 E-Mail info.sds@roche.com	Local representation:

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

Health Hazards:

3.1 Acute toxicity (Category 3)
H301 Toxic if swallowed.

3.7 Reproductive toxicity (Category 1B)
H360D May damage the unborn child.

Environmental Hazards:

4.1 Hazardous to the aquatic environment (Category 1)
H400 Very toxic to aquatic life.

4.1 Hazardous to the aquatic environment (Category 1)
H410 Very toxic to aquatic life with long lasting effects.

Signalword: Danger

Label:

Precautionary statements:

- P201 Obtain special instructions before use.
- P273 Avoid release to the environment.
- P301 + P310 IF SWALLOWED: Immediately call a POISON CENTER or doctor/physician.
- P309 + P310 IF exposed or if you feel unwell: Immediately call a POISON CENTER or doctor/physician.

2.3. Other hazards

Note

- may form explosible dust-air mixture if dispersed

SECTION 3: Composition/information on ingredients

Chemical name

- (S)-[3,4-Difluoro-2-(2-fluoro-4-iodophenylamino)phenyl][3-hydroxy-3-(piperidin-2-yl)azetidin-1-yl]methanone hemifumarate salt

Synonyms

- PAM07
- MEK Inhibitor (Hemifumarate Salt)
- XL518
- GDC-0973 Hemifumarate
- EXEL-5518
- PAM-RO5514041 (Fumarate)

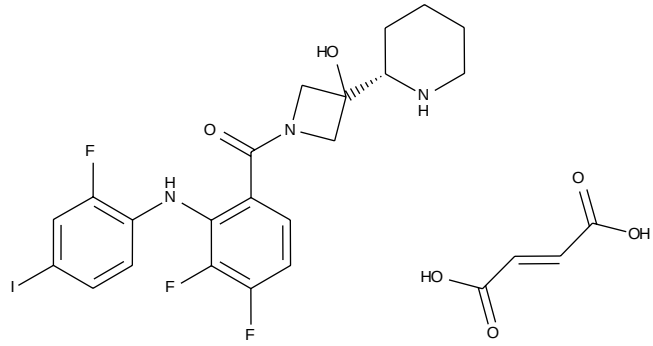
CAS number: 1369665-02-0

UN number: 2811

Roche number: RO5514041-001

Empirical formula: $C_{21}H_{21}F_3IN_3O_2 \bullet 1/2(C_4H_4O_4)$

Molecular mass	589.36 g/mol



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 - consult a physician
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

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	- formation of toxic combustion gases (hydrogen fluoride, nitrogen oxides) possible - consider dust explosion hazard

5.3. Advice for firefighters

Protection of fire-fighters	- precipitate gases/vapours/mists with water spray

SECTION 6: Accidental release measures

6.1. Personal precautions, protective equipment and emergency procedures

Personal precautions	- ensure adequate ventilation - avoid exposure

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 solids (avoid dust formation) and hand over to waste removal

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 electric charging of dust clouds - avoid dust formation; consider dust explosion hazard

7.2. Conditions for safe storage, including any incompatibilities

Storage conditions	- room temperature - protected from heat, light and humidity
Packaging materials	- tightly closing

SECTION 8: Exposure controls/personal protection

8.1. Control parameters

Threshold value (Roche) air	- IOEL (Internal Occupational Exposure Limit): 0.001 mg/m^3

8.2. Exposure controls

General protective and hygiene measures	- instruction of employees mandatory

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

SECTION 9: Physical and chemical properties

9.1. Information on basic physical and chemical properties

Colour	white to off-white
Form	crystalline powder
Odour	odourless
Solubility	740 mg/l, water 8’000 mg/l, methanol 880 mg/l, ethanol 190 mg/l, isopropanol 30 mg/l, acetonitrile
Partition coefficient	log P_{ow} 0.32 (octanol/water)
Melting temperature	234.8 °C

9.2. Other information

Dissociation constant	pK_1	1.98

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

Note	-	no information available

10.5. Incompatible materials

Note	-	no information available

10.6. Hazardous decomposition products

Note	-	not hygroscopic

SECTION 11: Toxicological information

11.1. Information on toxicological effects

Acute toxicity	-	LD_{50} > 60 to < 75 mg/kg (oral, rat) NOAEL 30 mg/kg (oral, rat)	*1
Subacute toxicity	-	NOAEL 1 mg/kg/d (oral, rat, 28 d)	*1
Subchronic toxicity	-	NOAEL 3 mg/kg/d (oral, rat; 13 weeks) LOAEL > 3 mg/kg/d (oral, rat; 13 weeks)	*1
Local effects	-	: no alert for irritation (in silico system)	*1
	-	: not phototoxic	*1
Sensitization	-	no information available	
Mutagenicity	-	not mutagenic (various in vitro test systems)	*1
Carcinogenicity	-	no information available	
Reproductive toxicity	-	teratogenic and embryotoxic	*1
STOT-single exposure	-	no information available	
STOT-repeated exposure	-	no information available	
Aspiration hazard	-	no information available	

1 referring to: Cobimetinib (free base)

SECTION 12: Ecological information

12.1. Toxicity

Ecotoxicity	-	moderately toxic for algae (Desmodesmus (=Scenedesmus) subspicatus) ErC_{50} (72 h) 11.8 mg/l (average measured concentration) NOErC (72 h) < 0.62 mg/l (average measured concentration) EyC_{50} (72 h) 2.25 mg/l (average measured concentration) NOEyC (72 h) < 0.62 mg/l (average measured concentration) (OECD No. 201)	*1

- strongly toxic for planktonic crustaceans (Daphnia magna)
  EC_{50} (48 h) 3.54 mg/l (average measured concentration)
  NOEC (48 h) 2.00 mg/l (average measured concentration)
  (OECD No. 202) *1
- highly toxic for fish (zebrafish)
  LC_{50} (96 h) 0.80 mg/l (average measured concentration)
  NOEC (96 h) 0.43 mg/l (average measured concentration)
  (OECD No. 203) *1
- no adverse influence on substrate biodegradation (activated sludge)
  concentration (28 d) 57.5 mg/l (measured initial concentration)
  (Manometric Respirometry Test, OECD No. 301 F) *1

12.2. Persistence and degradability

Ready biodegradability
- not readily biodegradable
  0 % BOD/ThOD, 28 d
  (Manometric Respirometry Test, OECD No. 301 F) *1

12.3. Bioaccumulative potential

Note
- no information available

12.4. Mobility in soil

Note
- no information available

12.5. Results of PBT and vPvB assessment

PBT/vPvB
- substance does not meet the criteria for PBT or vPvB

12.6. Other adverse effects

Air pollution
- observe local/national regulations

1 referring to: Cobimetinib (free base)

SECTION 13: Disposal considerations

13.1. Waste treatment methods

Waste from residues
- observe local/national regulations regarding waste disposal
- incinerate in qualified installation with flue gas scrubbing

SECTION 14: Transport information

IATA	Class	UN/ID	PG		PI	Label	Mark
	6.1	2811	III		670/677	6.1	EHS

IMDG	Class	UN	PG	EmS	PI	Label	Mark
	6.1	2811	III	F-A S-A	P002/IBC08	6.1	marine pollutant

RID/ADR	Class	UN	PG	Haz.no	PI	Label	Mark	Classif. code
	6.1	2811	III	60	P002/IBC08	6.1	EHS	T2

Proper shipping name TOXIC SOLID, ORGANIC, N.O.S.

Technical name Cobimetinib

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 (own classification according to directive VwVwS of 27.07.2005)

SECTION 16: Other information

Safety-lab number - BS10010

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.