

Safety Data Sheet

COTELLIC Tablets (20 mg)

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

1.1. Product identifier

Product name COTELLIC Tablets (20 mg)
Product code RO551-4041-F04
Synonyms - Cobimetinib F.C. Tablets 20 mg
- Cobimetinib Film Coated Tablets 20 mg
- Cobimetinib Tablets 20 mg

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

Use - pharmaceutical active substance (antineoplastic) *1

1.3. Details of the supplier of the safety data sheet

Company information Enquiries: Local representation:
Genentech, Inc.
1 DNA Way
South San Francisco
USA-CA 94080
United States of America

Phone 001-(650) 225-1000
E-Mail info.sds@roche.com
US Chemtrec phone:
(800)-424-9300

1.4. Emergency telephone number

Emergency telephone number US Chemtrec phone: (800)-424-9300

*1 referring to: Cobimetinib

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SECTION 2: Hazards identification

Classification of the substance or mixture / Label elements

GHS Classification

Health Hazards:

- 3.1 Acute toxicity (Category 4)
H302 Harmful if swallowed.
- 3.7 Reproductive toxicity (Category 1B)
H360D May damage the unborn child.

Signalword: Danger

Label:



Precautionary statements:

- P273 Avoid release to the environment.
- P301 + P312 IF SWALLOWED: Call a POISON CENTER/doctor/& if you feel unwell.

Other hazards

Note

- no information available

SECTION 3: Composition/information on ingredients

Characterization

pharmaceutical formulation of Cobimetinib

Chemical name

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

Ingredients

Concentration

**GHS-Classification
(pure ingredient)**

Cobimetinib

1369665-02-0

17.8 %

- Combustible dust (No category), USH003
- Acute toxicity (Category 3), H301
- Reproductive toxicity (Category 1B), H360D

Lactose monohydrate

57-11-4

29.2 %

Microcrystalline cellulose

9004-34-6

43.8 %

Croscarmellose sodium

74811-65-7

1.9 %

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Magnesium stearate 1.2 %
557-04-0

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

*1 referring to: Cobimetinib

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 - adapt extinguishing media to surrounding fire conditions
- Flash point (liquid) not applicable

5.2. Special hazards arising from the substance or mixture

Specific hazards - formation of toxic combustion gases (hydrogen fluoride, nitrogen oxides) possible

5.3. Advice for firefighters

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

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SECTION 6: Accidental release measures

6.1. Personal precautions, protective equipment and emergency procedures

Personal precautions - 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 - avoid dust formation

7.2. Conditions for safe storage, including any incompatibilities

Storage conditions - room temperature
- protected from heat, light and humidity

Packaging materials - tightly closing; material: metal (lined with polyethylene bag)

SECTION 8: Exposure controls/personal protection

8.1. Control parameters

Threshold value (USA) air	- ACGIH-TLV: 10 mg/m ³	*2
	- OSHA-PEL: 5 mg/m ³ (respirable dust fraction)	*2
	- OSHA-PEL: 15 mg/m ³ (total dust)	*2
	- NIOSH-REL: 5 mg/m ³ (respirable dust fraction)	*2
	- NIOSH-REL: 10 mg/m ³ (total dust)	*2
	- ACGIH-TLV: 10 mg/m ³	*3
Threshold value (Roche) air	- IOEL (Internal Occupational Exposure Limit): 0.001 mg/m ³	*1
PNEC	- 8.98 µg/l, surface freshwaters, based on chronic data	*4

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8.2. Exposure controls

Respiratory protection	- Respiratory protection is recommended as a precaution to minimize exposure. Effective engineering controls are considered to be the primary means to control worker exposure. Respiratory protection should not substitute for feasible engineering controls. - 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:	Cobimetinib
*2 referring to:	Microcrystalline cellulose
*3 referring to:	Magnesium stearate
*4 referring to:	Cobimetinib (free base)

SECTION 9: Physical and chemical properties

9.1. Information on basic physical and chemical properties

Color	white	
Form	tablets	
Empirical formula	$C_{21}H_{21}F_3IN_3O_2 \cdot 1/2(C_4H_4O_4)$	*1
Solubility	740 mg/l, water	*1
	8'000 mg/l, methanol	*1
	880 mg/l, ethanol	*1
	190 mg/l, isopropanol	*1
	30 mg/l, acetonitrile	*1
	insoluble, water (20 °C)	*2
Partition coefficient	log P _{ow} 0.32 (octanol/water)	*1
pH value (20 °C)	5 to 7.5 (100 g/l suspension in water)	*2
Melting temperature	234.8 °C	*1

9.2. Other information

Dissociation constant	pK ₁ 1.98	*1
*1 referring to:	Cobimetinib	
*2 referring to:	Microcrystalline cellulose	

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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
- sunlight

10.5. Incompatible materials

Note - no information available

10.6. Hazardous decomposition products

Note - not hygroscopic *1

*1 referring to: Cobimetinib

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)	*4
Subacute toxicity	- NOAEL 1 mg/kg/d (oral, rat, 28 d)	*4
Subchronic toxicity	- NOAEL 3 mg/kg/d (oral, rat; 13 weeks) LOAEL > 3 mg/kg/d (oral, rat; 13 weeks)	*4
Local effects	- not phototoxic	*4
Sensitization	- no information available	
Mutagenicity	- not mutagenic (various in vitro test systems)	*4
Carcinogenicity	- no information available	
Reproductive toxicity	- teratogenic and embryotoxic	*4

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STOT-single exposure	- no information available
STOT-repeated exposure	- no information available
Aspiration hazard	- no information available
Potential Health Effects	- Exposure: Inhalation, Ingestion, Skin contact, Eye contact - Carcinogenicity: not listed by NTP, IARC or OSHA
*4 referring to:	Cobimetinib (free base)

SECTION 12: Ecological information

12.1. Toxicity

Ecotoxicity	- moderately toxic for algae (<i>Desmodesmus subspicatus</i>) 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)	*4
	- strongly toxic for planktonic crustaceans (<i>Daphnia magna</i>) EC ₅₀ (48 h) 3.54 mg/l (average measured concentration) NOEC (48 h) 2.00 mg/l (average measured concentration) (OECD No. 202)	*4
	- 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)	*4
	- barely inhibitory on aerobic bacterial respiration (activated sludge) EC ₅₀ (3 h) > 1000 mg/l (nominal concentration) (OECD No. 209)	*4
	- <i>Daphnia magna</i> NOEC (21 d) 0.0898 mg/l (average measured concentration) (OECD No. 211)	*4
	- fish early life stage test (zebrafish) NOEC (35 d) ≥ 0.109 mg/l (OECD No. 210)	*4

12.2. Persistence and degradability

Ready biodegradability	- not readily biodegradable 0 % BOD/ThOD, 28 d (Manometric Respirometry Test, OECD No. 301 F)	*4
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12.3. Bioaccumulative potential

Note	- no information available
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12.4. Mobility in soil

Mobility - immobile (, 48 h, 20 °C)
 K_f = 77 to 110 ml/g (soil)
 K_f = 1167 ml/g (activated sludge, pH 6.0)
 K_{oc} = 2877 to 3799 l/kg (soil)
 K_d = 693 to 1244 l/kg (activated sludge)
 K_{oc} = 2356 to 5224 l/kg (activated sludge)
 (OECD No. 106 Adsorption/Desorption) *4

12.5. Results of PBT and vPvB assessment

PBT/vPvB - substance does not meet the criteria for PBT or vPvB *1

12.6. Other adverse effects

Note - no information available

*1 referring to: Cobimetinib
 *4 referring to: Cobimetinib (free base)

SECTION 13: Disposal considerations

13.1. Waste treatment methods

Waste from residues - return to supplier or hand over to authorized disposal company
 - observe local/national regulations regarding waste disposal
 - incinerate in qualified installation with flue gas scrubbing
 - DO NOT FLUSH unused medications or POUR them down a sink or drain. If available in your area, use takeback programs run by household hazardous waste collection programs or community pharmacies to dispose of unused and expired medicines. If you don't have access to a takeback program, dispose of these medicines in the household trash by removing them from their original containers and mixing them with an undesirable substance, such as used coffee grounds or kitty litter.

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

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RID/ADR	Class	UN	PG	Haz.no	PI	Label	Mark	Classif. code
	9	3077	III	90	P002/IBC08	9	EHS	M7
DOT	Class	UN/ID	PG	PI	RQ	Label	Haz.no	
	9	3077	III			9		
DOT Remark:		- NON-REGULATED IN NON-BULK PACKAGINGS TRANSPORTED BY MOTOR VEHICLES, RAIL CARS OR AIRCRAFT (49CFR 171.4(c)).						
Proper shipping name		ENVIRONMENTALLY HAZARDOUS SUBSTANCE, SOLID, N.O.S.						
Technical name		Cobimetinib						
SECTION 15: Regulatory information								
15.1. Safety, health and environmental regulations/legislation specific for the substance or mixture								
TSCA Status		- FDA Exemption - not on inventory						
Reporting Requirements		<ul style="list-style-type: none"> - The United States Environmental Protection Agency (USEPA) has not established a Reportable Quantity (RQ) for releases of this material. - In New Jersey, report all releases which enter a waterway or into soil, or which are likely to endanger the public health, harm the environment or cause a complaint to the NJDEPE Hotline and to local officials. - State and local regulations vary and may impose additional reporting requirements. 						
SECTION 16: Other information								
Safety-lab number		<ul style="list-style-type: none"> - BS10010 - BS10336 - BS10337 						*1
Full text of H-Statements referred to under section 3		<ul style="list-style-type: none"> H301 Toxic if swallowed. H360D May damage the unborn child. USH003 May form combustible dust concentrations in the air 						

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- Note - Please note this Safety Data Sheet for the bulk product does not apply for the finished, packaged medicinal product intended for the final user.
- Edition documentation - changes from previous version in sections 8, 12
- *1** referring to: Cobimetinib

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.