Safety Data Sheet

ZELBORAF(R) F.C. Tablets (240 mg)

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

1.1. Product identifier

Product name	ZELBORAF(R) F.C. Tablets (240 mg)
Product code	SAP-10122762
Synonyms	- ZELBORAF film-coated tablets - ZELBORAF F.C. Tablets

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: 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	Local representation:

1.4. Emergency telephone number

Emergency telephone number	US Chemtrec phone: (800)-424-9300
*1 referring to:	Vemurafenib

SECTION 2: Hazards identification

Classification of the substance or mixture / Label elements

GHS Classification	no classification and labelling according to GHS

Other hazards

Note	- no further information available

SECTION 3: Composition/information on ingredients

Characterization: Vemurafenib and other inactive ingredients

Ingredients	Concentration
Vemurafenib CAS: 918504-65-1	~ 28 %
Silicon dioxide [SiO2] CAS: 7631-86-9	~ 1 %
Polyvinyl alcohol CAS: 25213-24-5	0.9 %
Titanium dioxide CAS: 13463-67-7	0.6 %

SECTION 4: First aid measures

4.1. Description of first aid measures

Eye contact
- rinse with tap water for 10 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
- 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
- adapt extinguishing media to surrounding fire conditions
- water spray jet, dry powder, foam, carbon dioxide

Flash point (liquid): not applicable

5.2. Special hazards arising from the substance or mixture

Specific hazards	- very high probability of ignition of dust whirled up	*1
	- severe dust explosion hazard	*1
	- formation of toxic and corrosive combustion gases (hydrogen chloride, hydrogen fluoride, nitrogen oxides) possible	*1
	- substance is hazardous for water: contain fire-fighting wastewater	*1
	- Toxic emissions may be given off in a fire	

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	

*1 referring to: Vemurafenib

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)	*1
	- avoid dust formation; high dust explosion hazard	*1
	- high probability of ignition: ground plant, avoid effective ignition sources; avoid electrostatic charging of dust clouds	*1
	- processing in closed systems, if possible superposed by inert gas (e.g. nitrogen)	*2
	- avoid dust formation; high dust explosion hazard	*2
	- low probability of ignition: ground plant, avoid effective ignition sources	*2

7.2. Conditions for safe storage, including any incompatibilities

Storage conditions	- keep containers tightly closed - below 30 °C - protected from humidity	
Packaging materials	- high density polyethylene (HDPE) bottles with a child-resistant polypropylene screw cap	

*1 referring to: Vemurafenib
*2 referring to: SAC-HPMC-AS LG ex3rd SUC

SECTION 8: Exposure controls/personal protection

8.1. Control parameters

Threshold value (USA) air	- ACGIH-TLV: 10.0 mg/m3 (total dust) - OSHA-PEL: 6.00 mg/m3 (total dust) - ACGIH-TLV: 10 mg/m3 - OSHA-PEL: 15 mg/m3 (total dust)	*3 *3 *4 *4
Threshold value (Roche) air	- IOEL (Internal Occupational Exposure Limit): 0.015 mg/m3	*1

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	
Body protection	- wear conductive shoes	

*1 referring to: Vemurafenib
*3 referring to: Silicon dioxide [SiO2]
*4 referring to: Titanium dioxide

SECTION 9: Physical and chemical properties

9.1. Information on basic physical and chemical properties

Color	pinkish white to orange white	
Form	oval, biconvex tablet	
Solubility	0.00271 mg/l, water (20 °C, pH 8, OECD No. 105) ≤ 6.1 mg/l, aquatic ecotoxicity media (25 °C, HPLC)	*1 *1

Partition coefficient	log P_{ow} 4.74 pH 5	*1
	log P_{ow} 3.80 pH 7	*1
	log P_{ow} 3.26 pH 9	*1
	(HPLC Method, OECD No. 117)	
Melting temperature	272 °C	*1

9.2. Other information

Note - no information available

*1 referring to: Vemurafenib

SECTION 10: Stability and reactivity

10.1. Reactivity

Note - no information available

10.2. Chemical stability

Stability - stable under the conditions mentioned in chapter 7

10.3. Possibility of hazardous reactions

Note - no information available

10.4. Conditions to avoid

Conditions to avoid	- humidity	*1
	- light	*1
	- warming	*1

10.5. Incompatible materials

Note - no information available

10.6. Hazardous decomposition products

Note	- strongly exothermic decomposition at higher temperatures (> 200 °C)	*2

*1 referring to: Vemurafenib
*2 referring to: SAC-HPMC-AS LG ex3rd SUC

SECTION 11: Toxicological information

11.1. Information on toxicological effects

Acute toxicity	- NOEL 1'000 mg/kg (oral, rat)	*1
	- LD_{50} > 2'500 mg/kg (oral, rat)	*2
Subacute toxicity	- NOAEL 1'000 mg/kg/d (oral, rat, 28 d)	*1
Local effects	- skin: non-irritant (rabbit; OECD No. 404)	*1
	- phototoxic (in vitro)	*1
Sensitization	- not skin sensitizing (guinea pig) (OECD No. 406)	*1
Subchronic toxicity	- NOAEL 450 mg/kg/d (oral, rat; 13 weeks)	*1
Mutagenicity	- not mutagenic (Ames test; OECD No. 471 (Salmonella typhimurium))	*1
	- not mutagenic (test system in vivo; OECD No. 474 (Micronucleus Test))	*1
Reproductive toxicity	- not teratogenic (oral, rat)	*1
	- not teratogenic (oral, rabbit); NOAEL is 450 mg/kg/d.	*1
	- not embryotoxic (150 mg/kg/d; oral, rabbit, female, 14 d); NOAEL = 150 mg/kg/d	*1
Potential Health Effects	- Exposure: Ingestion	
	- Acute Effects: Causes phototoxicity (skin irritation due to exposure to light)., May cause skin drying, itching, peeling and rashes., This material has not been tested as a whole; therefore, the information described below is based on one or more of its ingredients., May cause musculoskeletal effects., Signs and symptoms may include muscle weakness or pain and skeletal abnormalities., May cause loss of hair., May cause general body weakness, fatigue and nausea.	
	- Chronic Effects: May cause skin cancer.	
	- Carcinogenicity: formulation not listed by NTP, IARC or OSHA	
	- Carcinogenicity: IARC Gr3 not classifiable	*3
	- Carcinogenicity: IARC Gr2B possibly carcinogenic to humans	*4
	- Carcinogenicity: IARC Gr3 not classifiable	*5
Additional Health Information	- Conditions Aggravated: Hypersensitivity to this material and other materials in its chemical class.	

*1	referring to:	Vemurafenib
*2	referring to:	SAC-HPMC-AS LG ex3rd SUC
*3	referring to:	Silicon dioxide [SiO2]
*4	referring to:	Titanium dioxide
*5	referring to:	Polyvinyl alcohol

SECTION 12: Ecological information

12.1. Toxicity

Ecotoxicity

- strongly toxic for algae (Pseudokirchneriella subcapitata)
  ErC_{50} (72 h) 21.91 mg/l (nominal concentration)
  ErC_{50} (72 h) 2.832 mg/l (average measured concentration)
  NOEC (72 h) 0.156 mg/l (average measured concentration)
  (OECD No. 201) *1
- barely toxic for planktonic crustaceans (nominal concentration = 100 mg/l) (Daphnia magna)
  EC_{50} (48 h) > 100 mg/l (nominal concentration)
  NOEC (48 h) 0.27 mg/l
  (OECD No. 202) *1
- barely toxic for fish (nominal concentration = 100 mg/l) (guppy)
  LC_{50} (96 h) > 100 mg/l (nominal concentration)
  NOEC (96 h) $\geq$ 0.27 mg/l
  (OECD No. 203) *1
- daphnid reproduction test (Daphnia magna)
  NOEC (21 d) 0.0171 mg/l (average measured concentration)
  (OECD No. 211) *1
- fish early life stage test (zebrafish)
  NOEC (35 d) 1.63 mg/l (average measured concentration)
  (OECD No. 210) *1
- barely inhibitory on aerobic bacterial respiration (activated sludge)
  NOEC (3 h) 301 mg/l (nominal concentration)
  (OECD No. 209) *1

12.2. Persistence and degradability

Inherent biodegradability

- not inherently biodegradable
  < 10 %, 28 d
  (MITI Test II, OECD No. 302 C) *1

Environmental fate

- very persistent in a sediment/water fate test, no transformation products identified
  (OECD 308, Transformation in natural water/sediment systems) *1

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:
  $DT_{50} \leq 0.6$ d
  $DT_{90} \leq 2$ d
  (Bioconcentration: flow-through fish test; OECD no. 305) *1

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) *1

12.5. Results of PBT and vPvB assessment

PBT/vPvB - not PBT, not vPvB *1

12.6. Other adverse effects

Air pollution - observe local/national regulations

*1 referring to: Vemurafenib

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
- 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

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: Vemurafenib

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
- 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 are likely to endanger the public health, harm the environment or cause a complaint to the NJDEPE Hotline (1-609-292-5560) and to local officials.
- State and local regulations vary and may impose additional reporting requirements.

SECTION 16: Other information

Safety-lab number
- BS-9076 *1
- BS-9274 *1
- BS-9349 *1

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 1, 2, 7, 9, 10

*1 referring to: Vemurafenib

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.