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

1.1. Product identifier

Product name: COTELLC 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:
Genentech, Inc.
1 DNA Way
South San Francisco
USA-CA 94080
United States of America

Local representation:
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
# COTELLIC Tablets (20 mg)

## SECTION 2: Hazards identification

### Classification of the substance or mixture / Label elements

<table>
<thead>
<tr>
<th>GHS Classification</th>
<th>Health Hazards:</th>
<th>Signalword: Danger</th>
</tr>
</thead>
</table>
| 3.1 Acute toxicity (Category 4) | 3.1 Acute toxicity (Category 4)  
H302 Harmful if swallowed.  
3.7 Reproductive toxicity (Category 1B)  
H360D May damage the unborn child. | - |

### 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)azetidin-1-yl]methanone hemifumarate salt

### Ingredients

<table>
<thead>
<tr>
<th>Ingredients</th>
<th>Concentration</th>
<th>GHS-Classification (pure ingredient)</th>
</tr>
</thead>
</table>
| Cobimetinib                        | 17.8 %        | - Combustible dust (No category), USH003  
- Acute toxicity (Category 3), H301  
- Reproductive toxicity (Category 1B), H360D |
| Lactose monohydrate                | 29.2 %        |                                        |
| Microcrystalline cellulose         | 43.8 %        |                                        |
| Croscarmellose sodium              | 1.9 %         |                                        |
**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
## 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$^3$  
- OSHA-PEL: 5 mg/m$^3$ (respirable dust fraction)  
- OSHA-PEL: 15 mg/m$^3$ (total dust)  
- NIOSH-REL: 5 mg/m$^3$ (respirable dust fraction)  
- NIOSH-REL: 10 mg/m$^3$ (total dust)  
- ACGIH-TLV: 10 mg/m$^3$  

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

**PNEC**
- 8.98 µg/l, surface freshwaters, based on chronic data

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Replacing edition of: 28.12.17  
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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  \( \text{C}_{21}\text{H}_{21}\text{F}_3\text{IN}_3\text{O}_2 \cdot \frac{1}{2}\text{(C}_4\text{H}_4\text{O}_4) \)  *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
\( \text{pK}_1 1.98 \) *1

*1 referring to: Cobimetinib
*2 referring to: Microcrystalline cellulose
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 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
COTELLIC Tablets (20 mg)

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 (Desmodesmus subspicatus)
ErC₅₀ (72 h) 11.8 mg/l (average measured concentration)
NOErC (72 h) < 0.62 mg/l (average measured concentration)
EyC₅₀ (72 h) 2.25 mg/l (average measured concentration)
NOEyC (72 h) < 0.62 mg/l (average measured concentration)
(OECD No. 201)

- strongly toxic for planktonic crustaceans (Daphnia magna)
EC₅₀ (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)
LC₅₀ (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)
EC₅₀ (3 h) > 1000 mg/l (nominal concentration)
(OECD No. 209) *4

- Daphnia magna
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

12.3. Bioaccumulative potential

Note - no information available
12.4. Mobility in soil

Mobility - immobile (, 48 h, 20 °C)
Kf = 77 to 110 ml/g (soil)
Kf = 1167 ml/g (activated sludge, pH 6.0)
KOC = 2877 to 3799 l/kg (soil)
Kd = 693 to 1244 l/kg (activated sludge)
KOC = 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

<table>
<thead>
<tr>
<th>IATA</th>
<th>Class</th>
<th>UN/ID</th>
<th>PG</th>
<th>PI</th>
<th>Label</th>
<th>Mark</th>
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</thead>
<tbody>
<tr>
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<td>3077</td>
<td>III</td>
<td></td>
<td>956/956</td>
<td>9</td>
<td>EHS</td>
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</table>

<table>
<thead>
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<th>Class</th>
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<tbody>
<tr>
<td>9</td>
<td>3077</td>
<td>III</td>
<td></td>
<td>F-A S-F</td>
<td>P002/IBC08</td>
<td>9</td>
<td>marine pollutant</td>
</tr>
</tbody>
</table>
COTELLIC Tablets (20 mg)

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 - 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 - BS10010
- BS10336
- BS10337

Full text of H-Statements referred to under section 3
H301 Toxic if swallowed.
H360D May damage the unborn child.
USH003 May form combustible dust concentrations in the air

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