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

Enquiries: info.sds@roche.com
Phone: 001-(650) 225-1000
E-Mail: info.sds@roche.com

Local representation:

US Chemtrec phone:
(800)-424-9300

1.4. Emergency telephone number

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

*1 referring to: Cobimetinib
## SECTION 2: Hazards identification

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

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

Signalword: Danger

### Label:

![Material hazard symbol](image)

Precautionary statements:
- P273 Avoid release to the environment.
- P301 + P312 IF SWALLOWED: Call a POISON CENTER or doctor/physician 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>
<tbody>
<tr>
<td>Cobimetinib 1369665-02-0</td>
<td>17.8 %</td>
<td>- Combustible dust (No category), USH003</td>
</tr>
<tr>
<td></td>
<td></td>
<td>- Acute toxicity (Category 3), H301</td>
</tr>
<tr>
<td></td>
<td></td>
<td>- Reproductive toxicity (Category 1B), H360D</td>
</tr>
<tr>
<td>Lactose monohydrate 57-11-4</td>
<td>29.2 %</td>
<td></td>
</tr>
<tr>
<td>Microcrystalline cellulose 9004-34-6</td>
<td>43.8 %</td>
<td></td>
</tr>
<tr>
<td>Croscarmellose sodium 74811-65-7</td>
<td>1.9 %</td>
<td></td>
</tr>
</tbody>
</table>
### 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$^3$
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

SECTION 9: Physical and chemical properties

9.1. Information on basic physical and chemical properties

Color
white

Form
tablets

Empirical formula
\( \text{C}_{21}\text{H}_{21}\text{F}_{3}\text{N}_{3}\text{O}_{2} \cdot 1/2(\text{C}_{4}\text{H}_{4}\text{O}_{4}) \)  

Solubility
- 740 mg/l, water  
- 8'000 mg/l, methanol  
- 880 mg/l, ethanol  
- 190 mg/l, isopropanol  
- 30 mg/l, acetonitrile  
- insoluble, water (20 °C)

Partition coefficient
\( \log P_{\text{ow}} 0.32 \) (octanol/water)

\( \text{pH value} \quad (20 \degree \text{C}) \)
5 to 7.5 (100 g/l suspension in water)

Melting temperature
234.8 °C

9.2. Other information

Dissociation constant
\( \text{pK}_1 1.98 \)  

\*1 referring to: Cobimetinib
\*2 referring to: Microcrystalline cellulose

SECTION 10: Stability and reactivity

10.1. Reactivity

Note
- no information available
**COTELLIC Tablets (20 mg)**

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

<table>
<thead>
<tr>
<th>Effect Type</th>
<th>Parameter</th>
<th>Value</th>
<th>Notes</th>
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</thead>
<tbody>
<tr>
<td>Acute toxicity</td>
<td>LD&lt;sub&gt;50&lt;/sub&gt;</td>
<td>&gt; 60 to &lt; 75 mg/kg (oral, rat)</td>
<td>*4</td>
</tr>
<tr>
<td></td>
<td>NOAEL</td>
<td>30 mg/kg (oral, rat)</td>
<td>*4</td>
</tr>
<tr>
<td>Subacute toxicity</td>
<td>NOAEL</td>
<td>1 mg/kg/d (oral, rat, 28 d)</td>
<td>*4</td>
</tr>
<tr>
<td>Subchronic toxicity</td>
<td>NOAEL</td>
<td>3 mg/kg/d (oral, rat; 13 weeks)</td>
<td>*4</td>
</tr>
<tr>
<td></td>
<td>LOAEL</td>
<td>&gt; 3 mg/kg/d (oral, rat; 13 weeks)</td>
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<tr>
<td>Local effects</td>
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<td>not phototoxic</td>
<td>*4</td>
</tr>
<tr>
<td>Sensitization</td>
<td></td>
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<td></td>
</tr>
<tr>
<td>Mutagenicity</td>
<td></td>
<td>not mutagenic (various in vitro test systems)</td>
<td>*4</td>
</tr>
<tr>
<td>Carcinogenicity</td>
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<td></td>
</tr>
<tr>
<td>Reproductive toxicity</td>
<td></td>
<td>teratogenic and embryotoxic</td>
<td>*4</td>
</tr>
<tr>
<td>STOT-single exposure</td>
<td></td>
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</tr>
<tr>
<td>STOT-repeated exposure</td>
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<tr>
<td>Aspiration hazard</td>
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</table>

Date: 25.5.16/LS (SEISMO)  Replacing edition of: 21.5.15  Page: 6/9
COTELLIC Tablets (20 mg)

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 (=Scenedesmus) subspicatus)
  - ErC<sub>50</sub> (72 h) 11.8 mg/l (average measured concentration)
  - NOErC (72 h) < 0.62 mg/l (average measured concentration)
  - EyC<sub>50</sub> (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)
  - EC<sub>50</sub> (48 h) 3.54 mg/l (average measured concentration)
  - NOEC (48 h) 2.00 mg/l (average measured concentration)
  (OECD No. 202)
- highly toxic for fish (zebrafish)
  - LC<sub>50</sub> (96 h) 0.80 mg/l (average measured concentration)
  - NOEC (96 h) 0.43 mg/l (average measured concentration)
  (OECD No. 203)
- 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)

*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

**Note**
- no information available

#### 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

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<th>PI</th>
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<td>III</td>
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<td>S-F</td>
<td>P002/IBC08</td>
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<td>marine pollutant</td>
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<tbody>
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<td>3077</td>
<td>III</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>9</td>
</tr>
</tbody>
</table>

DOT Remark:
- NON-REGULATED IN NON-BULK PACKAGINGS TRANSPORTED BY MOTOR VEHICLES, RAIL CARS OR AIRCRAFT (49CFR 171.4(c)).
COTELLIC Tablets (20 mg)

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
- R&D 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 (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  - 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 9

*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.