SECTION 1. IDENTIFICATION

Product name : ROZLYTREK Oral Pellets 50 mg

Product code : RO710-2122/F15

Common name(s), synonym(s) of the substance : Entrectinib with other ingredients

BS11491

Manufacturer or supplier’s details

Company name of supplier : Genentech, Inc.

Address : 1 DNA Way
South San Francisco, CA 94080
USA

Telephone : 001-(650) 225-1000

E-mail address : info.sds@roche.com

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

Recommended use of the chemical and restrictions on use

Recommended use : Formulated pharmaceutical active substance

Restrictions on use : For professional users only.
SAFETY DATA SHEET

ROZLYTREK Oral Pellets 50 mg

Version 1.2
Revision Date: 10-25-2023
Date of last issue: 10-23-2023
Date of first issue: 07-11-2023

P280 Wear protective gloves/ protective clothing/ eye protection/ face protection.

Response:
P305 + P351 + P338 IF IN EYES: Rinse cautiously with water for several minutes. Remove contact lenses, if present and easy to do. Continue rinsing.
P308 + P313 IF exposed or concerned: Get medical advice/ attention.
P337 + P313 If eye irritation persists: Get medical advice/ attention.

Storage:
P405 Store locked up.

Disposal:
P501 Dispose of contents/ container to an approved waste disposal plant.

Other hazards
None known.

SECTION 3. COMPOSITION/INFORMATION ON INGREDIENTS

Substance / Mixture : Mixture

Components

<table>
<thead>
<tr>
<th>Chemical name</th>
<th>CAS-No.</th>
<th>Concentration (% w/w)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Entrectinib</td>
<td>1108743-60-7</td>
<td>24</td>
</tr>
<tr>
<td>Cellulose</td>
<td>9004-34-6</td>
<td>45.7</td>
</tr>
<tr>
<td>D-Mannitol</td>
<td>69-65-8</td>
<td>9.6</td>
</tr>
<tr>
<td>Butanedioic acid, 2,3-dihydroxy-(2R,3R)-</td>
<td>87-69-4</td>
<td>7.1</td>
</tr>
<tr>
<td>Croscarmellose sodium</td>
<td>74811-65-7</td>
<td>6.5</td>
</tr>
<tr>
<td>sodium octadecyl fumarate</td>
<td>4070-80-8</td>
<td>1.7</td>
</tr>
<tr>
<td>Titanium oxide (TiO2)</td>
<td>13463-67-7</td>
<td>&lt;= 1.2</td>
</tr>
<tr>
<td>Aerosil 200</td>
<td>7631-86-9</td>
<td>1.1</td>
</tr>
<tr>
<td>Octadecanoic acid, magnesium salt (2:1)</td>
<td>557-04-0</td>
<td>0.4</td>
</tr>
<tr>
<td>non hazardous compounds</td>
<td>Not Assigned</td>
<td>&lt; 3</td>
</tr>
</tbody>
</table>

SECTION 4. FIRST AID MEASURES

General advice : Move out of dangerous area.
Show this material safety data sheet to the doctor in attendance.
Do not leave the victim unattended.

If inhaled : Move to fresh air.
If unconscious, place in recovery position and seek medical advice.
If symptoms persist, call a physician.
In case of skin contact: If on skin, rinse well with water.

In case of eye contact:
- Immediately flush eye(s) with plenty of water.
- Remove contact lenses.
- Protect unharmed eye.
- Keep eye wide open while rinsing.
- If eye irritation persists, consult a specialist.

If swallowed:
- Keep respiratory tract clear.
- Do not give milk or alcoholic beverages.
- Never give anything by mouth to an unconscious person.
- If symptoms persist, call a physician.
- Rinse mouth with water.

Most important symptoms and effects, both acute and delayed:
- Causes serious eye irritation.
- Suspected of causing cancer.

Notes to physician:
- The first aid procedure should be established in consultation with the doctor responsible for industrial medicine.

SECTION 5. FIRE-FIGHTING MEASURES

Suitable extinguishing media:
- Use extinguishing measures that are appropriate to local circumstances and the surrounding environment.

Unsuitable extinguishing media:
- High volume water jet

Specific hazards during fire fighting:
- Do not allow run-off from fire fighting to enter drains or water courses.

Hazardous combustion products:
- Carbon oxides
- In case of fire hazardous decomposition products may be produced such as:
  - Nitrogen oxides (NOx)
  - Fluorinated hydrocarbons

Further information:
- Collect contaminated fire extinguishing water separately. This must not be discharged into drains.
- Fire residues and contaminated fire extinguishing water must be disposed of in accordance with local regulations.

Special protective equipment for fire-fighters:
- Wear self-contained breathing apparatus for firefighting if necessary.

SECTION 6. ACCIDENTAL RELEASE MEASURES

Personal precautions, protective equipment and emergency procedures:
- Use personal protective equipment.
- Avoid dust formation.
- Avoid breathing dust.

Environmental precautions:
- Prevent product from entering drains.
- Prevent further leakage or spillage if safe to do so.
SAFETY DATA SHEET

ROZLYTREK Oral Pellets 50 mg

Methods and materials for containment and cleaning up: Keep in suitable, closed containers for disposal.

SECTION 7. HANDLING AND STORAGE

Advice on protection against fire and explosion: Avoid dust formation. Provide appropriate exhaust ventilation at places where dust is formed.

Advice on safe handling: Avoid formation of respirable particles. Do not breathe vapors/dust. Avoid contact with skin and eyes. For personal protection see section 8. Smoking, eating and drinking should be prohibited in the application area. Dispose of rinse water in accordance with local and national regulations.

Conditions for safe storage: Keep container tightly closed in a dry and well-ventilated place. Containers which are opened must be carefully resealed and kept upright to prevent leakage. Electrical installations / working materials must comply with the technological safety standards.

Further information on storage conditions: See label, package insert or internal guidelines.

Storage temperature: Protected from heat and light. Store at room temperature.

Further information on storage stability: No decomposition if stored and applied as directed.

Packaging material: Suitable material: Polyethylene bag in metal drum, Plastic container of HDPE, PVC, Blister packages.

SECTION 8. EXPOSURE CONTROLS/PERSONAL PROTECTION

Ingredients with workplace control parameters

<table>
<thead>
<tr>
<th>Components</th>
<th>CAS-No.</th>
<th>Value type (Form of exposure)</th>
<th>Control parameters / Permissible concentration</th>
<th>Basis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cellulose</td>
<td>9004-34-6</td>
<td>TWA</td>
<td>10 mg/m³</td>
<td>ACGIH</td>
</tr>
<tr>
<td></td>
<td></td>
<td>TWA (Respirable)</td>
<td>5 mg/m³</td>
<td>NIOSH REL</td>
</tr>
<tr>
<td></td>
<td></td>
<td>TWA (total)</td>
<td>10 mg/m³</td>
<td>NIOSH REL</td>
</tr>
<tr>
<td></td>
<td></td>
<td>TWA (total dust)</td>
<td>15 mg/m³</td>
<td>OSHA Z-1</td>
</tr>
<tr>
<td></td>
<td></td>
<td>TWA (respirable fraction)</td>
<td>5 mg/m³</td>
<td>OSHA Z-1</td>
</tr>
<tr>
<td></td>
<td></td>
<td>TWA (Total)</td>
<td>15 mg/m³</td>
<td>OSHA P0</td>
</tr>
</tbody>
</table>
**Predicted No Effect Concentration (PNEC):**

<table>
<thead>
<tr>
<th>Substance name</th>
<th>Environmental Compartment</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Entrectinib</td>
<td>Surface waters</td>
<td>0.3 µg/l</td>
</tr>
</tbody>
</table>

**Remarks:**
- Based on chronic data

**Engineering measures:**
- No data available

**Personal protective equipment**
- Hand protection

In case of contact through splashing:
SAFETY DATA SHEET

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Material: Nitrile rubber
Break through time: > 30 min
Glove thickness: > 0.11 mm

In case of full contact:
Material: butyl-rubber
Break through time: > 480 min
Glove thickness: > 0.4 mm

Remarks: Wear appropriate protective gloves to prevent skin contact. Replace torn or punctured gloves promptly.

Eye protection: Eye wash bottle with pure water
Tightly fitting safety goggles
Wear face-shield and protective suit for abnormal processing problems.

Skin and body protection: Dust impervious protective suit
Choose body protection according to the amount and concentration of the dangerous substance at the work place.

Hygiene measures: When using do not eat or drink.
When using do not smoke.
Wash hands before breaks and at the end of workday.

SECTION 9. PHYSICAL AND CHEMICAL PROPERTIES

Appearance: pellets
Color: orange
Odor: Not applicable
Odor Threshold: Not applicable
pH: Not applicable
Melting point/range: No data available
Boiling point/boiling range: No data available
Evaporation rate: No data available
Self-ignition: No data available
Upper explosion limit / Upper flammability limit: No data available
Lower explosion limit / Lower flammability limit: No data available
Vapor pressure: No data available
Relative vapor density : Not applicable
Relative density : No data available
Solubility(ies)
  Water solubility : No data available
  Solubility in other solvents : No data available
Autoignition temperature : No data available
Decomposition temperature : No data available
Viscosity
  Viscosity, dynamic : Not applicable
  Viscosity, kinematic : Not applicable

SECTION 10. STABILITY AND REACTIVITY
Reactivity : No dangerous reaction known under conditions of normal use.
Chemical stability : Stable under normal conditions.
Possibility of hazardous reactions : No decomposition if stored and applied as directed.
Conditions to avoid : No data available
Incompatible materials : No data available
Hazardous decomposition products : No data available

SECTION 11. TOXICOLOGICAL INFORMATION

Acute toxicity
Not classified based on available information.

Product:
Acute oral toxicity : Acute toxicity estimate: > 5,000 mg/kg
Method: Calculation method

Acute inhalation toxicity : Acute toxicity estimate: > 200 mg/l
Exposure time: 4 h
Test atmosphere: dust/mist
Method: Calculation method

Acute dermal toxicity : Acute toxicity estimate: > 5,000 mg/kg
Method: Calculation method
Components:

Cellulose:
Acute oral toxicity : LD50 Oral (Rat): > 5,000 mg/kg
Acute dermal toxicity : LD50 Dermal (Rabbit): > 2,000 mg/kg

Entrectinib:
Acute oral toxicity : LD50 Oral (Rat): > 2,000 mg/kg

Titanium oxide (TiO2):
Acute oral toxicity : LD50 (Rat): > 5,000 mg/kg
Method: OECD Test Guideline 425

Acute inhalation toxicity : LC50 (Rat): > 6.82 mg/l
Exposure time: 4 h
Test atmosphere: dust/mist

Acute dermal toxicity : LD50 (Rabbit): > 5,000 mg/kg

Aerosil 200:
Acute oral toxicity : LD50 (Rat, male and female): > 5,000 mg/kg
GLP: yes

Acute inhalation toxicity : LC50 (Rat, male and female): > 5.01 mg/l
Exposure time: 4 h
Test atmosphere: dust/mist
Method: OECD Test Guideline 436
GLP: yes
Assessment: The substance or mixture has no acute inhalation toxicity

Acute dermal toxicity : LD50 Dermal (Rabbit): > 5,000 mg/kg
Method: No information available.
GLP: No information available.

Octadecanoic acid, magnesium salt (2:1):
Acute oral toxicity : LD50 Oral (Rat): > 2,000 mg/kg

Skin corrosion/irritation
Not classified based on available information.

Product:
Remarks : May cause skin irritation in susceptible persons.

Components:

Entrectinib:
Species : Rabbit
Result : No skin irritation
### Butanediolic acid, 2,3-dihydroxy- (2R,3R)-:

**Remarks**: Extremely corrosive and destructive to tissue.

### Titanium oxide (TiO2):

- **Species**: Rabbit
- **Method**: OECD Test Guideline 404
- **Result**: No skin irritation

### Aerosil 200:

- **Species**: Rabbit
- **Exposure time**: 4 h
- **Method**: OECD Test Guideline 404
- **Result**: No skin irritation

**GLP**: No information available.

### Serious eye damage/eye irritation

Causes serious eye irritation.

**Product**:

**Remarks**: May cause irreversible eye damage.

### Components:

#### Entrectinib:

- **Species**: Rabbit
- **Result**: Mild eye irritation

#### Butanediolic acid, 2,3-dihydroxy- (2R,3R)-:

- **Result**: Risk of serious damage to eyes.
- **Remarks**: May cause irreversible eye damage.

#### Titanium oxide (TiO2):

- **Species**: Rabbit
- **Result**: No eye irritation
- **Method**: OECD Test Guideline 405

#### Aerosil 200:

- **Species**: Rabbit
- **Result**: No eye irritation
- **Exposure time**: 24 h
- **GLP**: no

### Respiratory or skin sensitization

#### Skin sensitization

Not classified based on available information.

#### Respiratory sensitization

Not classified based on available information.
Components:

Titanium oxide (TiO2):
Species: Guinea pig
Assessment: Does not cause skin sensitization.
Method: OECD Test Guideline 406

Aerosil 200:
Species: Guinea pig
Assessment: Does not cause skin sensitization.
Method: OECD Test Guideline 406
Result: Did not cause sensitization on laboratory animals.

Germ cell mutagenicity
Not classified based on available information.

Components:

Entrectinib:
Genotoxicity in vitro: Result: negative
Genotoxicity in vivo: Result: negative

Aerosil 200:
Genotoxicity in vitro:
Test Type: Microbial mutagenesis assay (Ames test)
Test system: Salmonella typhimurium
Metabolic activation: with and without metabolic activation
Method: OECD Test Guideline 471
Result: negative
GLP: yes

Test Type: Microbial mutagenesis assay (Ames test)
Test system: Escherichia coli
Metabolic activation: with and without metabolic activation
Method: OECD Test Guideline 471
Result: negative
GLP: yes

Test Type: In vitro mammalian cell gene mutation test
Test system: mouse lymphoma cells
Metabolic activation: with and without metabolic activation
Method: OECD Test Guideline 490
Result: negative
GLP: yes

Genotoxicity in vivo:
Species: Rat (male)
Cell type: Bone marrow
Application Route: Oral
Method: OECD Test Guideline 475
Result: negative
GLP: no
Carcinogenicity
Suspected of causing cancer.

Components:

Cellulose:
Remarks: No ingredient of this product present at levels greater than or equal to 0.1% is identified as probable, possible or confirmed human carcinogen by IARC.

Aerosil 200:
Species: Rat, male and female
Application Route: Oral
Exposure time: 2 Years
Method: No information available.
Result: negative
GLP: No information available.

IARC Group 2B: Possibly carcinogenic to humans
Titanium oxide (TiO2) 13463-67-7

OSHA No component of this product present at levels greater than or equal to 0.1% is on OSHA’s list of regulated carcinogens.

NTP No ingredient of this product present at levels greater than or equal to 0.1% is identified as a known or anticipated carcinogen by NTP.

Reproductive toxicity
Not classified based on available information.

Components:

Entrectinib:
Effects on fetal development: Species: Rat
Result: May lead to malformations at dose levels that cause maternal toxicity

Aerosil 200:
Effects on fertility: Species: Rat, male and female
Application Route: Oral
Dose: 100, 300, 1000 mg/kg bw/day
General Toxicity Parent: NOAEL: >= 1,000 mg/kg body weight
General Toxicity F1: NOAEL: >= 1,000 mg/kg body weight
Method: OECD Test Guideline 416
GLP: yes

Effects on fetal development: Species: Mouse, female
Application Route: Oral
Dose: 13.4, 62.3, 289, 1340 mg/kg bw/day
Duration of Single Treatment: 6 - 15 d
General Toxicity Maternal: LOAEL: >= 1,340 mg/kg bw/day
Embryo-fetal toxicity: NOAEL: >= 1,340 µg/kg body weight
Method: No information available.
GLP: No information available.
STOT-single exposure
Not classified based on available information.

Components:
Butanedioic acid, 2,3-dihydroxy- (2R,3R)-:
Assessment  :  The substance or mixture is not classified as specific target organ toxicant, single exposure.

Octadecanoic acid, magnesium salt (2:1):
Assessment  :  The substance or mixture is not classified as specific target organ toxicant, single exposure.

STOT-repeated exposure
Not classified based on available information.

Components:
Butanedioic acid, 2,3-dihydroxy- (2R,3R)-:
Assessment  :  The substance or mixture is not classified as specific target organ toxicant, repeated exposure.

Octadecanoic acid, magnesium salt (2:1):
Assessment  :  The substance or mixture is not classified as specific target organ toxicant, repeated exposure.

Repeated dose toxicity

Components:
Aerosil 200:
Species  :  Rat, male and female
NOEL  :  4000 mg/kg
Application Route  :  Oral
Exposure time  :  13 Weeks
Method  :  OECD Test Guideline 408
GLP  :  yes

Aspiration toxicity
Not classified based on available information.

Components:
Butanedioic acid, 2,3-dihydroxy- (2R,3R)-:
No data available

Octadecanoic acid, magnesium salt (2:1):
No data available
**Further information**

**Components:**

**Entrectinib:**
- Remarks: Phototoxic (in vitro)

### SECTION 12. ECOLOGICAL INFORMATION

**Ecotoxicity**

**Components:**

**Cellulose:**

**Ecotoxicology Assessment**

- Acute aquatic toxicity: This product has no known ecotoxicological effects.
- Chronic aquatic toxicity: This product has no known ecotoxicological effects.

**Entrectinib:**

- Toxicity to daphnia and other aquatic invertebrates:
  - EC50 (Daphnia magna (Water flea)): > 100 mg/l
  - Exposure time: 48 h
  - Method: OECD Test Guideline 202
  - GLP: yes
  - Remarks: nominal concentration
  - NOEC (Daphnia magna (Water flea)): 0.266 mg/l
  - Exposure time: 48 h
  - Method: OECD Test Guideline 202
  - GLP: yes

- Toxicity to algae/aquatic plants:
  - ErC50 (Desmodesmus subspicatus (green algae)): > 100 mg/l
  - Exposure time: 72 h
  - Method: OECD Test Guideline 201
  - GLP: yes
  - Remarks: nominal concentration
  - EyC50 (Desmodesmus subspicatus (green algae)): > 100 mg/l
  - Exposure time: 72 h
  - Method: OECD Test Guideline 201
  - GLP: yes
  - Remarks: nominal concentration
  - NOEC (Desmodesmus subspicatus (green algae)): 0.197 mg/l
  - Exposure time: 72 h
  - Method: OECD Test Guideline 201
  - GLP: yes

- Toxicity to fish (Chronic toxicity):
  - EC10 (Danio rerio (zebra fish)): 0.00311 mg/l
  - Exposure time: 35 d
  - Method: OECD Test Guideline 210
  - GLP: yes
Remarks: average measured concentration

Toxicity to daphnia and other aquatic invertebrates (Chronic toxicity): EC10 (Daphnia magna (Water flea)): 0.0645 mg/l
Exposure time: 21 d
Method: OECD Test Guideline 211
GLP: yes
Remarks: average measured concentration

Toxicity to microorganisms: NOEC (activated sludge): 1,000 mg/l
Exposure time: 3 h
Method: OECD Test Guideline 209
GLP: yes
Remarks: nominal concentration

(activated sludge): Exposure time: 14 d
Method: OECD Test Guideline 301F
GLP: yes
Remarks: no adverse influence on substrate biodegradation

Butanedioic acid, 2,3-dihydroxy- (2R,3R)::-

Toxicity to fish: LC50 (Carassius auratus (goldfish)): 1,000 mg/l
Exposure time: 72 h

Toxicity to daphnia and other aquatic invertebrates: EC50 (Daphnia magna (Water flea)): 135 mg/l
Exposure time: 48 h

Ecotoxicology Assessment
Toxicity Data on Soil: Not expected to adsorb on soil.
Other organisms relevant to the environment: No data available

Titanium oxide (TiO2):
Toxicity to fish: LC50 (Pimephales promelas (fathead minnow)): > 1,000 mg/l
Exposure time: 96 h
Test Type: static test

LC50 (Cyprinodon variegatus (sheepshead minnow)): > 10,000 mg/l
Exposure time: 96 h
Test Type: semi-static test
Method: OECD Test Guideline 203

Toxicity to daphnia and other aquatic invertebrates: LC50 (Daphnia magna (Water flea)): > 1,000 mg/l
Exposure time: 48 h
Test Type: static test
Method: OECD Test Guideline 202

Toxicity to algae/aquatic plants: EC50 (Pseudokirchneriella subcapitata (green algae)): > 100 mg/l
Exposure time: 72 h
Test Type: static test
Method: OECD Test Guideline 201
## SAFETY DATA SHEET

### ROZLYTREK Oral Pellets 50 mg

<table>
<thead>
<tr>
<th>Version</th>
<th>Revision Date:</th>
<th>Date of last issue:</th>
<th>Date of first issue:</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.2</td>
<td>10-25-2023</td>
<td>10-23-2023</td>
<td>07-11-2023</td>
</tr>
</tbody>
</table>

**Ecotoxicology Assessment**

**Toxicity Data on Soil**: Not expected to adsorb on soil.

**Other organisms relevant to the environment**: No data available

### Aerosil 200:

**Toxicity to fish**: LC50 (Pimephales promelas (fathead minnow)): > 5,000 mg/l
- **End point**: mortality
- **Exposure time**: 96 h
- **Test Type**: static test
- **Analytical monitoring**: no
- **Method**: OECD Test Guideline 203
- **GLP**: no

**Toxicity to daphnia and other aquatic invertebrates**: EL50 (Daphnia magna (Water flea)): > 10,000 mg/l
- **End point**: Immobilization
- **Exposure time**: 24 h
- **Test Type**: static test
- **Analytical monitoring**: no
- **Method**: OECD Test Guideline 202
- **GLP**: yes

**Toxicity to algae/aquatic plants**: EC50 (Desmodesmus subspicatus (green algae)): > 173.1 mg/l
- **End point**: Growth rate
- **Exposure time**: 72 h
- **Test Type**: static test
- **Analytical monitoring**: yes
- **Method**: OECD Test Guideline 201
- **GLP**: yes

**Toxicity to daphnia and other aquatic invertebrates (Chronic toxicity)**: Lowest Observed Effect Concentration (Daphnia magna (Water flea)): 149.2 mg/l
- **End point**: mortality
- **Exposure time**: 21 d
- **Test Type**: semi-static test
- **Analytical monitoring**: yes
- **Method**: OECD Test Guideline 211
- **GLP**: yes

**Toxicity to microorganisms**: NOEC (activated sludge): 1,000 mg/l
- **End point**: Respiration inhibition
- **Exposure time**: 3 h
- **Test Type**: static test
SAFETY DATA SHEET

ROZLYTREK Oral Pellets 50 mg

Version 1.2
Revision Date: 10-25-2023
Date of last issue: 10-23-2023
Date of first issue: 07-11-2023

Analytical monitoring: no
Method: OECD Test Guideline 209
GLP: yes

Ecotoxicology Assessment
Toxicity Data on Soil: Not expected to adsorb on soil.
Other organisms relevant to the environment: No data available

Octadecanoic acid, magnesium salt (2:1):
Ecotoxicology Assessment
Acute aquatic toxicity: This product has no known ecotoxicological effects.
Chronic aquatic toxicity: This product has no known ecotoxicological effects.
Toxicity Data on Soil: Not expected to adsorb on soil.
Other organisms relevant to the environment: No data available

Persistence and degradability

Components:

Entrectinib:
Biodegradability: Result: Not readily biodegradable.
Biodegradation: < 10 %
Exposure time: 28 d
Method: OECD Test Guideline 301F
GLP: yes

Result: Primary biodegradation
Method: OECD Test Guideline 308
GLP: yes

Physico-chemical removability: Method: OECD Test Guideline 301F
Remarks: Not abiotically degradable

Titanium oxide (TiO2):
Biodegradability: Remarks: Not applicable

Aerosil 200:
Biodegradability: Remarks: Not applicable

Bioaccumulative potential

Components:

Cellulose:
Partition coefficient: n- Remarks: No data available
octanol/water

**Entrectinib:**

Bioaccumulation  
Species: Danio rerio (zebra fish)  
Bioconcentration factor (BCF): 217  
Exposure time: 20 d  
Temperature: 68 °F / 20 °C  
Concentration: 0.00162 mg/l  
Method: OECD Test Guideline 305  
GLP: yes  
Remarks: Does not significantly accumulate in organisms.

Partition coefficient: n-octanol/water  
\[
\text{log Pow}: 2.7 \ (68 \ °F / 20 \ °C) \\
pH: 5.0 \\
Method: OECD Test Guideline 107  
GLP: yes
\]

\[
\text{log Pow}: 4.3 \ (68 \ °F / 20 \ °C) \\
pH: 7.0 \\
Method: OECD Test Guideline 107  
GLP: yes
\]

\[
\text{log Pow}: 5.1 \ (68 \ °F / 20 \ °C) \\
pH: 9.0 \\
Method: OECD Test Guideline 107  
GLP: yes
\]

\[
\text{log Pow}: 4.43 \ (77 \ °F / 25 \ °C) \\
pH: 7.0 \\
Method: OECD Test Guideline 123  
GLP: yes
\]

**Butanedioic acid, 2,3-dihydroxy- (2R,3R)-:**

Partition coefficient: n-octanol/water  
\[
\text{log Pow}: < 1
\]

**Titanium oxide (TiO2):**

Partition coefficient: n-octanol/water  
Remarks: No data available

**Aerosil 200:**

Partition coefficient: n-octanol/water  
Remarks: Not applicable

**Octadecanoic acid, magnesium salt (2:1):**

Partition coefficient: n-octanol/water  
\[
\text{log Pow}: 0.8 \\
Method: OECD Test Guideline 107
\]
SAFETY DATA SHEET

ROZLYTREK Oral Pellets 50 mg

Mobility in soil

Components:

Entrectinib:
Distribution among environmental compartments: Medium: Soil
Koc: > 10000
Method: OECD Test Guideline 121

Stability in soil: Method: OECD Test Guideline 307
GLP: yes
Remarks: Primary biodegradation

Other adverse effects

Product:
Ozone-Depletion Potential: Regulation: 40 CFR Protection of Environment; Part 82 Protection of Stratospheric Ozone - CAA Section 602 Class I Substances
Remarks: This product neither contains, nor was manufactured with a Class I or Class II ODS as defined by the U.S. Clean Air Act Section 602 (40 CFR 82, Subpt. A, App.A + B).

Additional ecological information: An environmental hazard cannot be excluded in the event of unprofessional handling or disposal.
Very toxic to aquatic life with long lasting effects.

Components:

Entrectinib:
Results of PBT and vPvB assessment: This substance is not considered to be persistent, bioaccumulating and toxic (PBT). This substance is not considered to be very persistent and very bioaccumulating (vPvB).

SECTION 13. DISPOSAL CONSIDERATIONS

Disposal methods
Waste from residues: The product should not be allowed to enter drains, water courses or the soil.
Do not contaminate ponds, waterways or ditches with chemical or used container.
Send to a licensed waste management company.
Can be disposed as waste water, when in compliance with local regulations.

Contaminated packaging: Empty remaining contents.
Dispose of as unused product.
Empty containers should be taken to an approved waste handling site for recycling or disposal.
Do not re-use empty containers.
## SECTION 14. TRANSPORT INFORMATION

### International Regulations

#### UNRTDG

<table>
<thead>
<tr>
<th>Property</th>
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<tbody>
<tr>
<td>UN number</td>
<td>UN 3077</td>
</tr>
<tr>
<td>Proper shipping name</td>
<td>ENVIRONMENTALLY HAZARDOUS SUBSTANCE, SOLID, N.O.S. (Entrectinib mixture)</td>
</tr>
<tr>
<td>Class</td>
<td>9</td>
</tr>
<tr>
<td>Packing group</td>
<td>III</td>
</tr>
<tr>
<td>Labels</td>
<td>9</td>
</tr>
</tbody>
</table>

#### IATA-DGR

<table>
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<tr>
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<tr>
<td>Proper shipping name</td>
<td>Environmentally hazardous substance, solid, n.o.s. (Entrectinib mixture)</td>
</tr>
<tr>
<td>Class</td>
<td>9</td>
</tr>
<tr>
<td>Packing group</td>
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</tr>
<tr>
<td>Labels</td>
<td>Miscellaneous</td>
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<td>Packing instruction (cargo aircraft)</td>
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</tr>
<tr>
<td>Packing instruction (passenger aircraft)</td>
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<tr>
<td>Environmentally hazardous</td>
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#### IMDG-Code

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<tr>
<td>UN number</td>
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<tr>
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<td>ENVIRONMENTALLY HAZARDOUS SUBSTANCE, SOLID, N.O.S. (Entrectinib mixture)</td>
</tr>
<tr>
<td>Class</td>
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<td>Packing group</td>
<td>III</td>
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<tr>
<td>Labels</td>
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<tr>
<td>EmS Code</td>
<td>F-A, S-F</td>
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<tr>
<td>Marine pollutant</td>
<td>yes</td>
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</table>

### Transport in bulk according to Annex II of MARPOL 73/78 and the IBC Code

Not applicable

### Domestic regulation

#### 49 CFR

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<tr>
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<td>Class</td>
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<td>Labels</td>
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<td>Marine pollutant</td>
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### Special precautions for user

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<tr>
<td>Remarks</td>
<td>No data available</td>
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</tbody>
</table>

The transport classification(s) provided herein are for informational purposes only, and solely based upon the properties of the unpackaged material as it is described within this Safety Data.
SAFETY DATA SHEET

ROZLYTREK Oral Pellets 50 mg

Version 1.2
Revision Date: 10-25-2023
Date of last issue: 10-23-2023
Date of first issue: 07-11-2023

Sheet. Transportation classifications may vary by mode of transportation, package sizes, and variations in regional or country regulations.

SECTION 15. REGULATORY INFORMATION

CERCLA Reportable Quantity
This material does not contain any components with a CERCLA RQ.

SARA 304 Extremely Hazardous Substances Reportable Quantity
This material does not contain any components with a section 304 EHS RQ.

SARA 302 Extremely Hazardous Substances Threshold Planning Quantity
This material does not contain any components with a section 302 EHS TPQ.

SARA 311/312 Hazards:
- Carcinogenicity
- Serious eye damage or eye irritation

SARA 313:
This material does not contain any chemical components with known CAS numbers that exceed the threshold (De Minimis) reporting levels established by SARA Title III, Section 313.

Clean Air Act
This product neither contains, nor was manufactured with a Class I or Class II ODS as defined by the U.S. Clean Air Act Section 602 (40 CFR 82, Subpt. A, App.A + B). This product does not contain any hazardous air pollutants (HAP), as defined by the U.S. Clean Air Act Section 112 (40 CFR 61). This product does not contain any chemicals listed under the U.S. Clean Air Act Section 112(r) for Accidental Release Prevention (40 CFR 68.130, Subpart F). This product does not contain any chemicals listed under the U.S. Clean Air Act Section 111 SOCMI Intermediate or Final VOC's (40 CFR 60.489).

Clean Water Act
This product does not contain any Hazardous Substances listed under the U.S. CleanWater Act, Section 311, Table 116.4A. This product does not contain any Hazardous Chemicals listed under the U.S. CleanWater Act, Section 311, Table 117.3. This product does not contain any toxic pollutants listed under the U.S. Clean Water Act Section 307. This product does not contain any priority pollutants related to the U.S. Clean Water Act

US State Regulations

Massachusetts Right To Know
- Cellulose 9004-34-6
- Entrectinib 1108743-60-7
- Titanium oxide (TiO2) 13463-67-7
- Aerosil 200 7631-86-9

Pennsylvania Right To Know
- Cellulose 9004-34-6
- Entrectinib 1108743-60-7
- D-Mannitol 69-65-8
- Butanediolic acid, 2,3-dihydroxy- (2R,3R)- 87-69-4
- Croscarmellose sodium 74811-65-7
- Titanium oxide (TiO2) 13463-67-7
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Aerosil 200
7631-86-9

Maine Chemicals of High Concern
Entrectinib
1108743-60-7

Vermont Chemicals of High Concern
Entrectinib
1108743-60-7

Washington Chemicals of High Concern
Entrectinib
1108743-60-7

California Prop. 65
WARNING: This product can expose you to chemicals including Titanium dioxide, which is/are known to the State of California to cause cancer. For more information go to www.P65Warnings.ca.gov.

California List of Hazardous Substances
Aerosil 200
7631-86-9

California Permissible Exposure Limits for Chemical Contaminants
Cellulose
9004-34-6
Titanium oxide (TiO2)
13463-67-7
Aerosil 200
7631-86-9

The ingredients of this product are reported in the following inventories:

DSL: This product contains the following components that are not on the Canadian DSL nor NDSL.
   - Entrectinib
   - Croscarmellose sodium
   - non hazardous compounds
   - sodium octadecyl fumarate

AICS: Not in compliance with the inventory
NZIoC: Not in compliance with the inventory
ENCS: Not in compliance with the inventory
ISHL: Not in compliance with the inventory
KECI: Not in compliance with the inventory
PICCS: Not in compliance with the inventory
IECSC: Not in compliance with the inventory
TCSI: Not in compliance with the inventory
TSCA: Product contains substance(s) not listed on TSCA inventory.

TSCA list
No substances are subject to a Significant New Use Rule.
No substances are subject to TSCA 12(b) export notification requirements.

**SECTION 16. OTHER INFORMATION**

**NFPA 704:**

- Flammability: 0
- Health: 2
- Instability: 0
- Special hazard

**HMIS® IV:**

- HEALTH: *
- FLAMMABILITY: 0
- PHYSICAL HAZARD: 0

HMIS® ratings are based on a 0-4 rating scale, with 0 representing minimal hazards or risks, and 4 representing significant hazards or risks. The "*" represents a chronic hazard, while the "\(\)" represents the absence of a chronic hazard.

**Full text of other abbreviations**

- ACGIH: USA. ACGIH Threshold Limit Values (TLV)
- NIOSH REL: USA. NIOSH Recommended Exposure Limits
- OSHA CARC: OSHA Specifically Regulated Chemicals/Carcinogens
- OSHA P0: USA. Table Z-1-A Limits for Air Contaminants (1989 vacated values)
- OSHA Z-1: USA. Occupational Exposure Limits (OSHA) - Table Z-1 Limits for Air Contaminants
- OSHA Z-3: USA. Occupational Exposure Limits (OSHA) - Table Z-3 Mineral Dusts
- ACGIH / TWA: 8-hour, time-weighted average
- NIOSH REL / TWA: Time-weighted average concentration for up to a 10-hour workday during a 40-hour workweek
- OSHA CARC / PEL: Permissible exposure limit (PEL)
- OSHA P0 / TWA: 8-hour time weighted average
- OSHA Z-1 / TWA: 8-hour time weighted average
- OSHA Z-3 / TWA: 8-hour time weighted average

AIIC - Australian Inventory of Industrial Chemicals; ASTM - American Society for the Testing of Materials; bw - Body weight; CERCLA - Comprehensive Environmental Response, Compensation, and Liability Act; CMR - Carcinogen, Mutagen or Reproductive Toxicant; DIN - Standard of the German Institute for Standardisation; DOT - Department of Transportation; DSL - Domestic Substances List (Canada); ECx - Concentration associated with x% response; EHS - Extremely Hazardous Substance; ELx - Loading rate associated with x% response; EmS - Emergency Schedule; ENCS - Existing and New Chemical Substances (Japan); ErCx - Concentration associated with x% growth rate response; ERG - Emergency Response Guide; GHS - Globally Harmonized System; GLP - Good Laboratory Practice; HMIS - Hazardous Materials Identification System; IARC - International Agency for Research on Cancer; IATA - International Air Transport Association; IBC -
SAFETY DATA SHEET

ROZLYTREK Oral Pellets 50 mg

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- International Code for the Construction and Equipment of Ships carrying Dangerous Chemicals in Bulk; IC50 - Half maximal inhibitory concentration; ICAO - International Civil Aviation Organization; IECSC - Inventory of Existing Chemical Substances in China; IMDG - International Maritime Dangerous Goods; IMO - International Maritime Organization; ISHL - Industrial Safety and Health Law (Japan); ISO - International Organisation for Standardization; KECI - Korea Existing Chemicals Inventory; LC50 - Lethal Concentration to 50% of a test population; LD50 - Lethal Dose to 50% of a test population (Median Lethal Dose); MARPOL - International Convention for the Prevention of Pollution from Ships; MSHA - Mine Safety and Health Administration; n.o.s. - Not Otherwise Specified; NFPA - National Fire Protection Association; NO(A)EC - No Observed (Adverse) Effect Concentration; NO(A)EL - No Observed (Adverse) Effect Level; NOELR - No Observable Effect Loading Rate; NTP - National Toxicology Program; NZIoC - New Zealand Inventory of Chemicals; OECD - Organization for Economic Co-operation and Development; OPPTS - Office of Chemical Safety and Pollution Prevention; PBT - Persistent, Bioaccumulative and Toxic substance; PICCS - Philippines Inventory of Chemicals and Chemical Substances; (Q)SAR - (Quantitative) Structure Activity Relationship; RCRA - Resource Conservation and Recovery Act; REACH - Regulation (EC) No 1907/2006 of the European Parliament and of the Council concerning the Registration, Evaluation, Authorisation and Restriction of Chemicals; RQ - Reportable Quantity; SADT - Self-Accelerating Decomposition Temperature; SARA - Superfund Amendments and Reauthorization Act; SDS - Safety Data Sheet; TCSI - Taiwan Chemical Substance Inventory; TECI - Thailand Existing Chemicals Inventory; TSCA - Toxic Substances Control Act (United States); UN - United Nations; UNRTDG - United Nations Recommendations on the Transport of Dangerous Goods; vPvB - Very Persistent and Very Bioaccumulative

Revision Date : 10-25-2023

The information provided in this Safety Data Sheet is correct to the best of our knowledge, information and belief at the date of its publication. The information given is designed only as a guidance for safe handling, use, processing, storage, transportation, disposal and release and is not to be considered a warranty or quality specification. The information relates only to the specific material designated and may not be valid for such material used in combination with any other materials or in any process, unless specified in the text.

US / Z8 / 2204