

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

SECTION 1. IDENTIFICATION

Product name : ROZLYTREK Oral Pellets 50 mg

Product code : RO710-2122/F15

Common name(s), syno- : Entrectinib with other ingredients
nym(s) of the substance 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

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

Recommended use of the chemical and restrictions on use

Recommended use : Formulated pharmaceutical active substance

Restrictions on use : For professional users only.

SECTION 2. HAZARDS IDENTIFICATION

GHS classification in accordance with the OSHA Hazard Communication Standard (29 CFR 1910.1200)

Eye irritation : Category 2A

Carcinogenicity : Category 2

GHS label elements

Hazard pictograms :



Signal Word : Warning

Hazard Statements : H319 Causes serious eye irritation.
H351 Suspected of causing cancer.

Precautionary Statements : **Prevention:**
P201 Obtain special instructions before use.
P202 Do not handle until all safety precautions have been read and understood.
P264 Wash skin thoroughly after handling.

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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

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

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.

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- 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.

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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

Components	CAS-No.	Value type (Form of exposure)	Control parameters / Permissible concentration	Basis
Cellulose	9004-34-6	TWA	10 mg/m ³	ACGIH
		TWA (Respirable)	5 mg/m ³	NIOSH REL
		TWA (total)	10 mg/m ³	NIOSH REL
		TWA (total dust)	15 mg/m ³	OSHA Z-1
		TWA (respirable fraction)	5 mg/m ³	OSHA Z-1
		TWA (Total)	15 mg/m ³	OSHA P0

SAFETY DATA SHEET

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		dust)		
		TWA (respirable dust fraction)	5 mg/m3	OSHA P0
Entrectinib	1108743-60-7	IOEL	0.015 mg/m3	Roche Industrial Hygiene Committee (RIHC)
Titanium oxide (TiO2)	13463-67-7	TWA (total dust)	15 mg/m3	OSHA Z-1
		TWA (Total dust)	10 mg/m3	OSHA P0
		TWA (Respirable particulate matter)	0.2 mg/m3 (Titanium dioxide)	ACGIH
		TWA (Respirable particulate matter)	2.5 mg/m3 (Titanium dioxide)	ACGIH
Aerosil 200	7631-86-9	TWA (Dust)	20 Million particles per cubic foot (Silica)	OSHA Z-3
		TWA (Dust)	80 mg/m3 / %SiO2 (Silica)	OSHA Z-3
		TWA	6 mg/m3 (Silica)	NIOSH REL
		TWA (Respirable dust)	0.05 mg/m3 (Silica)	NIOSH REL
		PEL (respirable)	0.05 mg/m3	OSHA CARC
Octadecanoic acid, magnesium salt (2:1)	557-04-0	TWA (Inhalable particulate matter)	10 mg/m3	ACGIH
		TWA (Respirable particulate matter)	3 mg/m3	ACGIH

Predicted No Effect Concentration (PNEC):

Substance name	Environmental Compartment	Value
Entrectinib	Surface waters	0.3 µg/l
	Remarks: Based on chronic data	

Engineering measures : No data available

Personal protective equipment

Hand protection

In case of contact through splashing:

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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

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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 reac- : No decomposition if stored and applied as directed.
tions

Conditions to avoid : No data available

Incompatible materials : No data available

Hazardous decomposition : No data available
products

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

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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 425Acute 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: yesAcute 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 toxicityAcute 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

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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**Butanedioic 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.

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Species : Guinea pig
 Assessment : Does not cause skin sensitization.
 Method : OECD Test Guideline 406

Aerosil 200:

Test Type : Maximization Test
 Species : Guinea pig
 Assessment : Does not cause skin sensitization.
 Method : OECD Test Guideline 406
 Result : Did not cause sensitization on laboratory animals.
 GLP : yes

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

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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.

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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

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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 concentrationNOEC (Daphnia magna (Water flea)): 0.266 mg/l
Exposure time: 48 h
Method: OECD Test Guideline 202
GLP: yesToxicity 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 concentrationEyC50 (Desmodesmus subspicatus (green algae)): > 100 mg/l
Exposure time: 72 h
Method: OECD Test Guideline 201
GLP: yes
Remarks: nominal concentrationNOEC (Desmodesmus subspicatus (green algae)): 0.197 mg/l
Exposure time: 72 h
Method: OECD Test Guideline 201
GLP: yesToxicity to fish (Chronic toxicity) : EC10 (Danio rerio (zebra fish)): 0.00311 mg/l
Exposure time: 35 d
Method: OECD Test Guideline 210
GLP: yes

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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

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EC50 (Skeletonema costatum (marine diatom)): > 10,000 mg/l
Exposure time: 72 h
Method: ISO 10253

NOEC (Skeletonema costatum (marine diatom)): 5,600 mg/l
Exposure time: 72 h
Method: ISO 10253

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

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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 : log Pow: 2.7 (68 °F / 20 °C)
 pH: 5.0
 Method: OECD Test Guideline 107
 GLP: yes

log Pow: 4.3 (68 °F / 20 °C)
 pH: 7.0
 Method: OECD Test Guideline 107
 GLP: yes

log Pow: 5.1 (68 °F / 20 °C)
 pH: 9.0
 Method: OECD Test Guideline 107
 GLP: yes

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 : 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 : log Pow: 0.8
 Method: OECD Test Guideline 107

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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.

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SECTION 14. TRANSPORT INFORMATION

International Regulations

UNRTDG

UN number : UN 3077
 Proper shipping name : ENVIRONMENTALLY HAZARDOUS SUBSTANCE, SOLID,
 N.O.S.
 (Entrectinib mixture)
 Class : 9
 Packing group : III
 Labels : 9

IATA-DGR

UN/ID No. : UN 3077
 Proper shipping name : Environmentally hazardous substance, solid, n.o.s.
 (Entrectinib mixture)
 Class : 9
 Packing group : III
 Labels : Miscellaneous
 Packing instruction (cargo aircraft) : 956
 Packing instruction (passenger aircraft) : 956
 Environmentally hazardous : yes

IMDG-Code

UN number : UN 3077
 Proper shipping name : ENVIRONMENTALLY HAZARDOUS SUBSTANCE, SOLID,
 N.O.S.
 (Entrectinib mixture)
 Class : 9
 Packing group : III
 Labels : 9
 EmS Code : F-A, S-F
 Marine pollutant : yes

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

Not applicable

Domestic regulation

49 CFR

UN/ID/NA number : UN 3077
 Proper shipping name : Environmentally hazardous substance, solid, n.o.s.
 (Entrectinib mixture)
 Class : 9
 Packing group : III
 Labels : CLASS 9
 ERG Code : 171
 Marine pollutant : no

Special precautions for user

Remarks : No data available

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

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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 SOCM 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 (TiO ₂)	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
Butanedioic acid, 2,3-dihydroxy- (2R,3R)-	87-69-4
Croscarmellose sodium	74811-65-7
Titanium oxide (TiO ₂)	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.

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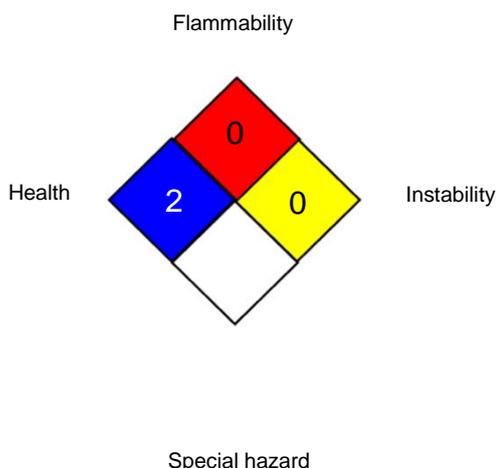
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No substances are subject to TSCA 12(b) export notification requirements.

SECTION 16. OTHER INFORMATION

NFPA 704:



HMIS® IV:

HEALTH	*	2
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

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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; TECl - 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

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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.

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