SAFETY DATA SHEET

1. IDENTIFICATION OF THE SUBSTANCE/MIXTURE AND THE COMPANY/UNDERTAKING

Product Identifier

Material Name: Lorlatinib Film Coated Tablets

Trade Name: LORVIQUA; LORBRENA
Synonyms: Lorlatinib
Chemical Family: Not determined

Relevant Identified Uses of the Substance or Mixture and Uses Advised Against

Intended Use: Pharmaceutical product

Details of the Supplier of the Safety Data Sheet

Pfizer Inc
Pfizer Pharmaceuticals Group
235 East 42nd Street
New York, New York 10017
1-800-879-3477

Emergency telephone number:
CHEMTREC (24 hours): 1-800-424-9300
Contact E-Mail: pfizer-MSDS@pfizer.com

Pfizer Ltd
Ramsgate Road
Sandwich, Kent
CT13 9NJ
United Kingdom
+00 44 (0)1304 616161

Emergency telephone number:
International CHEMTREC (24 hours): +1-703-527-3887

2. HAZARDS IDENTIFICATION

Classification of the Substance or Mixture

GHS - Classification

Germ Cell Mutagenicity: Category 2
Reproductive Toxicity: Category 2
Specific target organ systemic toxicity (repeated exposure): Category 2
Acute aquatic toxicity: Category 1
Chronic aquatic toxicity: Category 1

Label Elements

Signal Word: Warning
Hazard Statements: H341 - Suspected of causing genetic defects
H361d - Suspected of damaging the unborn child
H373 - May cause damage to organs through prolonged or repeated exposure pancreas, liver, spleen, central nervous system, skin
H410 - Very toxic to aquatic life with long lasting effects

Precautionary Statements:

P201 - Obtain special instructions before use
P260 - Do not breathe dust/fume/gas/mist/vapors/spray
P273 - Avoid release to the environment
P281 - Use personal protective equipment as required
P308 + P313 - IF exposed or concerned: Get medical attention/advice
P391 - Collect spillage
P405 - Store locked up
P501 - Dispose of contents/container in accordance with all local and national regulations

Other Hazards

An Occupational Exposure Value has been established for one or more of the ingredients (see Section 8).

Note:

This document has been prepared in accordance with standards for workplace safety, which requires the inclusion of all known hazards of the product or its ingredients regardless of the potential risk. The precautionary statements and warning included may not apply in all cases. Your needs may vary depending upon the potential for exposure in your workplace.

3. COMPOSITION / INFORMATION ON INGREDIENTS

Hazardous

Ingredient	CAS Number	EU EINECS/ELINCS List	GHS Classification	%
Lorlatinib	1454846-35-5	Not Listed	Muta.2 (H341) STOT RE.2 (H373) Repr 2 (H361d) Aquatic Acute 1 (H400) Aquatic Chronic 1 (H410)	5-10

Ingredient	CAS Number	EU EINECS/ELINCS List	GHS Classification	%
Microcrystalline cellulose	9004-34-6	232-674-9	Not Listed	*
Dicalcium Phosphate	7757-93-9	231-826-1	Not Listed	*
Sodium starch glycolate	9063-38-1	Not Listed	Not Listed	*
Magnesium Stearate	557-04-0	209-150-3	Not Listed	*

Additional Information:

* Proprietary
Ingredient(s) indicated as hazardous have been assessed under standards for workplace safety. In accordance with 29 CFR 1910.1200, the exact percentage composition of this mixture has been withheld as a trade secret.

For the full text of the CLP/GHS abbreviations mentioned in this Section, see Section 16

4. FIRST AID MEASURES

Description of First Aid Measures

Eye Contact: Flush with water while holding eyelids open for at least 15 minutes. Seek medical attention immediately.

Skin Contact: Remove contaminated clothing. Flush area with large amounts of water. Use soap. Seek medical attention.

Ingestion: Never give anything by mouth to an unconscious person. Wash out mouth with water. Do not induce vomiting unless directed by medical personnel. Seek medical attention immediately.

Inhalation: Remove to fresh air and keep patient at rest. Seek medical attention immediately.

Most Important Symptoms and Effects, Both Acute and Delayed

Symptoms and Effects of Exposure: For information on potential signs and symptoms of exposure, See Section 2 - Hazards Identification and/or Section 11 - Toxicological Information.

Medical Conditions Aggravated by Exposure: None known

Indication of the Immediate Medical Attention and Special Treatment Needed

Notes to Physician: None

5. FIRE FIGHTING MEASURES

Extinguishing Media: Extinguish fires with CO2, extinguishing powder, foam, or water.

Special Hazards Arising from the Substance or Mixture

Hazardous Combustion Products: Formation of toxic gases is possible during heating or fire. May include oxides of carbon and nitrogen and products of fluorine.

Fire / Explosion Hazards: Fine particles (such as dust and mists) may fuel fires/explosions.

Advice for Fire-Fighters

During all firefighting activities, wear appropriate protective equipment, including self-contained breathing apparatus.

6. ACCIDENTAL RELEASE MEASURES

Personal Precautions, Protective Equipment and Emergency Procedures

Personnel involved in clean-up should wear appropriate personal protective equipment (see Section 8). Minimize exposure.

Environmental Precautions

Place waste in an appropriately labeled, sealed container for disposal. Care should be taken to avoid environmental release.

Methods and Material for Containment and Cleaning Up

Measures for Cleaning / Collecting: Contain the source of spill if it is safe to do so. Collect spilled material by a method that controls dust generation. A damp cloth or a filtered vacuum should be used to clean spills of dry solids. Clean spill area thoroughly.

Additional Consideration for Large Spills: Non-essential personnel should be evacuated from affected area. Report emergency situations immediately. Cleanup operations should only be undertaken by trained personnel.

7. HANDLING AND STORAGE

Precautions for Safe Handling

7. HANDLING AND STORAGE

Minimize dust generation and accumulation. If tablets or capsules are crushed and/or broken, avoid breathing dust and avoid contact with eyes, skin, and clothing. When handling, use appropriate personal protective equipment (see Section 8). Wash thoroughly after handling. Releases to the environment should be avoided. Refer to Section 12 - Ecological Information, for information on potential effects on the environment. Review and implement appropriate technical and procedural waste water and waste disposal measures to prevent occupational exposure or environmental releases. Potential points of process emissions of this material to the atmosphere should be controlled with dust collectors, HEPA filtration systems or other equivalent controls.

Conditions for Safe Storage, Including any Incompatibilities

Storage Conditions: Store as directed by product packaging.

Specific end use(s): Pharmaceutical drug product

8. EXPOSURE CONTROLS / PERSONAL PROTECTION

Control Parameters

Refer to available public information for specific member state Occupational Exposure Limits.

Lorlatinib

Pfizer OEL TWA-8 Hr:	10 µg/m^3

Microcrystalline cellulose

ACGIH Threshold Limit Value (TWA)	10 mg/m^3
Australia TWA	10 mg/m^3
Belgium OEL - TWA	10 mg/m^3
Estonia OEL - TWA	10 mg/m^3
France OEL - TWA	10 mg/m^3
Ireland OEL - TWAs	10 mg/m^3 4 mg/m^3
Latvia OEL - TWA	2 mg/m^3
OSHA - Final PELS - TWAs:	15 mg/m^3
Portugal OEL - TWA	10 mg/m^3
Romania OEL - TWA	10 mg/m^3
Russia OEL - TWA	6 mg/m^3
Spain OEL - TWA	10 mg/m^3
Switzerland OEL -TWAs	3 mg/m^3
Vietnam OEL - TWAs	10 mg/m^3 5 mg/m^3

Dicalcium Phosphate

Latvia OEL - TWA	10 mg/m^3

Magnesium Stearate

Lithuania OEL - TWA	5 mg/m^3
Sweden OEL - TWAs	5 mg/m^3

Exposure Controls

Engineering Controls: Engineering controls should be used as the primary means to control exposures. General room ventilation is adequate unless the process generates dust, mist or fumes. Keep airborne contamination levels below the exposure limits listed above in this section.

Personal Protective Equipment: Refer to applicable national standards and regulations in the selection and use of personal protective equipment (PPE). Contact your safety and health professional or safety equipment supplier for assistance in selecting the correct protective clothing/equipment based on an assessment of the workplace conditions, other chemicals used or present in the workplace and specific operational processes.

8. EXPOSURE CONTROLS / PERSONAL PROTECTION

Hands: Impervious disposable gloves (e.g. Nitrile, etc.) (double recommended) if skin contact with drug product is possible and for bulk processing operations. (Protective gloves must meet the standards in accordance with EN374, ASTM F1001 or international equivalent.)

Eyes: Wear safety glasses or goggles if eye contact is possible. (Eye protection must meet the standards in accordance with EN166, ANSI Z87.1 or international equivalent.)

Skin: Impervious disposable protective clothing is recommended if skin contact with drug product is possible and for bulk processing operations. (Protective clothing must meet the standards in accordance with EN13982, ANSI 103 or international equivalent.)

Respiratory protection: Under normal conditions of use, if the applicable Occupational Exposure Limit (OEL) is exceeded, wear an appropriate respirator with a protection factor sufficient to control exposures to below the OEL (e.g. particulate respirator with a full mask, P3 filter). (Respirators must meet the standards in accordance with EN136, EN143, ASTM F2704-10 or international equivalent.)

9. PHYSICAL AND CHEMICAL PROPERTIES

Physical State: Solid
Color: Tan to Light purple
Odor: No data available.
Odor Threshold: No data available.
Molecular Formula: C21 H19 F N6 O2
Molecular Weight: 406.15

Solvent Solubility: No data available
Water Solubility: No data available
pH: No data available.
Melting/Freezing Point (°C): No data available
Boiling Point (°C): No data available.
Partition Coefficient: (Method, pH, Endpoint, Value)
Microcrystalline cellulose
No data available
Dicalcium Phosphate
No data available
Sodium starch glycolate
No data available
Magnesium Stearate
No data available
Lorlatinib
Measured 7 Log P 2.47
Decomposition Temperature (°C): No data available.

Evaporation Rate (Gram/s): No data available
Vapor Pressure (kPa): No data available
Vapor Density (g/ml): No data available
Relative Density: No data available
Viscosity: No data available

Flammablity:
Autoignition Temperature (Solid) (°C): No data available
Flammability (Solids): No data available
Flash Point (Liquid) (°C): No data available
Upper Explosive Limits (Liquid) (% by Vol.): No data available
Lower Explosive Limits (Liquid) (% by Vol.): No data available

10. STABILITY AND REACTIVITY

Reactivity: No data available

10. STABILITY AND REACTIVITY

Chemical Stability: Stable under normal conditions of use.
Possibility of Hazardous Reactions
Oxidizing Properties: No data available
Conditions to Avoid: Fine particles (such as dust and mists) may fuel fires/explosions. As a precautionary measure, keep away from heat sources and electrostatic discharge.
Incompatible Materials: As a precautionary measure, keep away from strong oxidizers
Hazardous Decomposition Products: No data available

11. TOXICOLOGICAL INFORMATION

Information on Toxicological Effects
General Information: Toxicological properties have not been thoroughly investigated.
Short Term: May produce slight eye irritation. (based on components)
Known Clinical Effects: Based on clinical trials in humans, possible adverse effects following exposure to this compound may include: Hypercholesterolemia, effects on central nervous system, and sensory/motor nerve injury (peripheral neuropathy).

Acute Toxicity: (Species, Route, End Point, Dose)

Microcrystalline cellulose
Rat Oral LD50 > 5000 mg/kg
Rabbit Dermal LD50 > 2000 mg/kg

Lorlatinib
Rat Oral NOAEL 100 mg/kg
Acute Toxicity Comments: A greater than symbol (>) indicates that the toxicity endpoint being tested was not achievable at the highest dose used in the test.

Irritation / Sensitization: (Study Type, Species, Severity)

Microcrystalline cellulose
Skin Irritation Rabbit Non-irritating
Eye Irritation Rabbit Non-irritating

Lorlatinib
Skin Corrosivity (*In vitro* , RHE) Not applicable Negative
Eye Irritation (*In vitro* , BCOP) Not applicable Negative
Skin Irritation Rabbit Negative
Eye Irritation Rabbit Minimal
Skin Sensitization - LLNA Mouse Negative

Repeated Dose Toxicity: (Duration, Species, Route, Dose, End Point, Target Organ)

Magnesium Stearate
13 Week(s) Rat Oral 1092 g/kg LOAEL Liver

Lorlatinib
2 Week(s) Rat Oral 6 (3 BID) mg/kg/day NOAEL Male reproductive system, Pancreas, Liver
2 Week(s) Dog Oral 5 mg/kg/day NOAEL Cardiovascular system, Gastrointestinal system
1 Month(s) Rat Oral (M) 8/ (F) 4 mg/kg/day NOAEL Pancreas, Liver, Spleen, Central Nervous System, Skin
1 Month(s) Dog Oral 25 (12.5 BID) mg/kg/day NOAEL None identified

11. TOXICOLOGICAL INFORMATION

13 Week(s) Rat Oral (M) 8 / (F) 4 mg/kg/day NOAEL Kidney, Pancreas, Skin
13 Week(s) Dog Oral 7 (3.5 BID) mg/kg/day NOAEL Lungs Bone Liver Lymphatic system Thymus Skin Spleen Male reproductive system

Reproduction & Development Toxicity: (Duration, Species, Route, Dose, End Point, Effect(s))

Lorlatinib

Embryo / Fetal Development	Rat	Oral	4 mg/kg/day	NOAEL	Maternal toxicity
Embryo / Fetal Development	Rat	Oral	1 mg/kg/day	LOAEL	Developmental toxicity
Embryo / Fetal Development	Rabbit	Oral	4 mg/kg/day	NOAEL	Maternal Toxicity
Embryo / Fetal Development	Rabbit	Oral	1 mg/kg/day	NOAEL	Developmental toxicity

Genetic Toxicity: (Study Type, Cell Type/Organism, Result)

Lorlatinib
Bacterial Mutagenicity (Biolum Ames) *Salmonella* Negative
In Vitro Micronucleus TK6 lymphoblastoid cells Positive
In Vitro Micronucleus Chinese Hamster Ovary (CHO) cells Negative
In Vivo Micronucleus Rat Bone Marrow Positive
Bacterial Mutagenicity (Ames) *Salmonella* , *E. coli* Negative

Genetic Toxicity Comments: **PF-06463922:** The above genetic toxicity studies (Biolum Ames) were preliminary assays. Investigation into the mechanism of the positive response in the In Vivo Micronucleus Assay suggests an aneugenic rather than clastogenic mechanism.

Carcinogen Status: None of the components of this formulation are listed as a carcinogen by IARC, NTP or OSHA.

12. ECOLOGICAL INFORMATION

Environmental Overview: Releases to the environment should be avoided. Environmental properties have not been thoroughly investigated.

Toxicity:
Aquatic Toxicity: (Species, Method, End Point, Duration, Result)

Lorlatinib
Cyprinodon variegatus (Sheepshead Minnow) OECD LC50 96 Hours 37 mg/L
Tisbe battagliai (Marine Copepod) OECD LC50 48 Hours 2.2 mg/L
Skeletonema costatum (Marine Diatom) OECD ErC50 72 Hours 11 mg/L

Bacterial Inhibition: (Inoculum, Method, End Point, Result)

Lorlatinib
Activated sludge OECD EC50 > 1000 mg/L

Chronic Aquatic Toxicity: (Species, Method, Duration, Endpoint, Result, Adverse Endpoint)

Lorlatinib
Pimephales promelas (Fathead Minnow) OECD 33 Day(s) NOEC 5.2 ug/L Survival
Daphnia magna (Water Flea) OECD 21 Day(s) NOEC 0.99 ug/L Reproduction

Persistence and Degradability:

Biodegradation: (Method, Inoculum, Biodeg Study, Result, Endpoint, Duration, Classification)
Lorlatinib
OECD Activated sludge Ready 64% After 28 Day(s) Not Ready

Bio-accumulative Potential:
Partition Coefficient: (Method, pH, Endpoint, Value)
Lorlatinib
Measured 7 Log P 2.47

Mobility in Soil:
Sorption: (Method, Inoculum, Sorption Endpoint, Endpoint, Results)
Lorlatinib
OECD Activated sludge Adsorption KOC 212
OECD Sediment Adsorption 7344

13. DISPOSAL CONSIDERATIONS

Waste Treatment Methods: Dispose of waste in accordance with all applicable laws and regulations. Member State specific and Community specific provisions must be considered. Considering the relevant known environmental and human health hazards of the material, review and implement appropriate technical and procedural waste water and waste disposal measures to prevent occupational exposure and environmental release. It is recommended that waste minimization be practiced. The best available technology should be utilized to prevent environmental releases. This may include destructive techniques for waste and wastewater.

14. TRANSPORT INFORMATION

The following refers to all modes of transportation unless specified below.

This material is regulated for transportation as a hazardous material/dangerous good.

UN number: UN 3077
UN proper shipping name: Environmentally Hazardous Substance, Solid, n.o.s (Lorlatinib)
Transport hazard class(es): 9
Packing group: III
Environmental Hazard(s): Marine Pollutant

5 kg/5L Exception:
5 kg/5L Exception:
UN3082 and UN3077 materials contained in good quality packaging in the quantities listed below are not regulated as dangerous goods for transport by any mode:

* Single packagings containing a net quantity of 5 liters or less for liquids or a net mass of 5 kg or less for solids.
* Combination packagings containing a net quantity per inner packaging of 5 liters or less for liquids or a net mass of 5 kg or less for solids.

15. REGULATORY INFORMATION

Safety, Health and Environmental Regulations/Legislation Specific for the Substance or Mixture

15. REGULATORY INFORMATION

Lorlatinib

CERCLA/SARA 313 Emission reporting	Not Listed
California Proposition 65	Not Listed
EU EINECS/ELINCS List	Not Listed

Microcrystalline cellulose

CERCLA/SARA 313 Emission reporting	Not Listed
California Proposition 65	Not Listed
Inventory - United States TSCA - Sect. 8(b)	Present
Australia (AICS):	Present
EU EINECS/ELINCS List	232-674-9

Dicalcium Phosphate

CERCLA/SARA 313 Emission reporting	Not Listed
California Proposition 65	Not Listed
Inventory - United States TSCA - Sect. 8(b)	Present
Australia (AICS):	Present
EU EINECS/ELINCS List	231-826-1

Sodium starch glycolate

CERCLA/SARA 313 Emission reporting	Not Listed
California Proposition 65	Not Listed
Inventory - United States TSCA - Sect. 8(b)	Present
Australia (AICS):	Present
EU EINECS/ELINCS List	Not Listed

Magnesium Stearate

CERCLA/SARA 313 Emission reporting	Not Listed
California Proposition 65	Not Listed
Inventory - United States TSCA - Sect. 8(b)	Present
Australia (AICS):	Present
EU EINECS/ELINCS List	209-150-3

16. OTHER INFORMATION

Text of CLP/GHS Classification abbreviations mentioned in Section 3

Germ cell mutagenicity-Cat.2; H341 - Suspected of causing genetic defects
Specific target organ toxicity, repeated exposure-Cat.2; H373 - May cause damage to organs through prolonged or repeated exposure
Reproductive toxicity-Cat.2; H361d - Suspected of damaging the unborn child
Hazardous to the aquatic environment, acute toxicity-Cat.1; H400 - Very toxic to aquatic life
Hazardous to the aquatic environment, chronic toxicity-Cat.1; H410 - Very toxic to aquatic life with long lasting effects

Data Sources: Pfizer proprietary drug development information. Publicly available toxicity information.

Reasons for Revision: Updated Section 1 - Identification of the Substance/Preparation and the Company/Undertaking.
Updated Section 11 - Toxicology Information.

Revision date: 07-Sep-2018

Product Stewardship Hazard Communication

Prepared by: Pfizer Global Environment, Health, and Safety Operations

Pfizer Inc believes that the information contained in this Safety Data Sheet is accurate, and while it is provided in good faith, it is without warranty of any kind, expressed or implied. If data for a hazard are not included in this document there is no known information at this time.

End of Safety Data Sheet