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

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

Contact E-Mail: pfizer-MSDS@pfizer.com

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

PZ03144
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

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

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

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/m³

Microcrystalline cellulose
ACGIH Threshold Limit Value (TWA) 10 mg/m³
Australia TWA 10 mg/m³
Belgium OEL - TWA 10 mg/m³
Estonia OEL - TWA 10 mg/m³
France OEL - TWA 10 mg/m³
Ireland OEL - TWA 10 mg/m³
Latvia OEL - TWA 4 mg/m³
OSHA - Final PELS - TWA: 15 mg/m³
Portugal OEL - TWA 10 mg/m³
Romania OEL - TWA 10 mg/m³
Russia OEL - TWA 6 mg/m³
Spain OEL - TWA 10 mg/m³
Switzerland OEL - TWA 3 mg/m³
Vietnam OEL - TWA 10 mg/m³

Dicalcium Phosphate
Latvia OEL - TWA 10 mg/m³

Magnesium Stearate
Lithuania OEL - TWA 5 mg/m³
Sweden OEL - TWA 5 mg/m³

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
Odor: No data available.
Molecular Formula: C21 H19 F N6 O2

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) No data available.

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

Flammability:
- 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

**Genetic Toxicity:**

*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:**

*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:**

*Activated sludge* OECD EC50 > 1000 mg/L

**Chronic Aquatic Toxicity:**

*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.
SAFETY DATA SHEET

Material Name:  Lorlatinib Film Coated Tablets
Revision date: 07-Sep-2018
Prepared by:  Product Stewardship Hazard Communication
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