SAFETY DATA SHEET

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

Product Identifier

Material Name: Crizotinib Capsules

Trade Name: XALKORI, CRIZALK
Chemical Family: Anaplastic Lymphoma Kinase Inhibitor

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

Intended Use: Pharmaceutical product for the treatment of lung cancer

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

Serious Eye Damage/Eye Irritation: Category 1
Skin Sensitization: Category 1
Germ Cell Mutagenicity: Category 2
Acute aquatic toxicity: Category 1

Label Elements

Signal Word: Danger
Hazard Statements: H318 - Causes serious eye damage
H317 - May cause an allergic skin reaction
H341 - Suspected of causing genetic defects
H400 - Very toxic to aquatic life

Precautionary Statements:

P280 - Wear protective gloves/protective clothing/eye protection/face protection
P305 + P351 + P338 - IF IN EYES: Rinse cautiously with water for several minutes. Remove contact lenses, if present and easy to do. Continue rinsing
P310 - Immediately call a POISON CENTRE or doctor/physician
P261 - Avoid breathing dust/fume/gas/mist/vapors/spray
P272 - Contaminated work clothing must not be allowed out of the workplace
P302+ P352 - IF ON SKIN: Wash with plenty of soap and water
P333 + P313 - If skin irritation or rash occurs: Get medical advice/attention
P321 - Specific treatment (see supplemental instructions on the administration of antidotes on this label)
P363 - Wash contaminated clothing before reuse
P202 - Do not handle until all safety precautions have been read and understood
P308 + P313 - IF exposed or concerned: Get medical attention/advice
P405 - Store locked up
P273 - Avoid release to the environment
P391 - Collect spillage
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	%
Crizotinib	877399-52-5	Not Listed	Eye Dam.1 (H318) Skin Sens.1 (H317) Muta. 2 (H341) Aquatic Acute 1 (H400)	50
Dicalcium Phosphate	7757-93-9	231-826-1	Not Listed	*
Microcrystalline cellulose	9004-34-6	232-674-9	Not Listed	*
Magnesium stearate	557-04-0	209-150-3	Not Listed	*
Ferric oxide red	1309-37-1	215-168-2	Not Listed	*
Titanium dioxide	13463-67-7	236-675-5	Not Listed	*

Ingredient	CAS Number	EU EINECS/ELINCS List	GHS Classification	%
Sodium starch glycolate	9063-38-1	Not Listed	Not Listed	*

Gelatin	9000-70-8	232-554-6	Not Listed	*
Silicium dioxide	Not Assigned	Not Listed	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.

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

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. 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. Refer to Section 12 - Ecological Information, for information on potential effects on the environment.

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.

Crizotinib

Pfizer OEL TWA-8 Hr:	15µg/m^3, Sensitizer, Severe Eye Irritant

Dicalcium Phosphate

Latvia OEL - TWA	10 mg/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

Magnesium stearate

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

Ferric oxide red

8. EXPOSURE CONTROLS / PERSONAL PROTECTION

ACGIH Threshold Limit Value (TWA)	5 mg/m^3
Australia TWA	5 mg/m^3
	10 mg/m^3
Austria OEL - MAKs	5 mg/m^3
	10 mg/m^3
Belgium OEL - TWA	5 mg/m^3
Bulgaria OEL - TWA	5.0 mg/m^3
Denmark OEL - TWA	3.5 mg/m^3
Estonia OEL - TWA	3.5 mg/m^3
Finland OEL - TWA	5 mg/m^3
France OEL - TWA	5 mg/m^3
Greece OEL - TWA	10 mg/m^3
Hungary OEL - TWA	6 mg/m^3
Ireland OEL - TWAs	5 mg/m^3
	10 mg/m^3
	4 mg/m^3
Lithuania OEL - TWA	3.5 mg/m^3
OSHA - Final PELS - TWAs:	10 mg/m^3
	15 mg/m^3
Poland OEL - TWA	5 mg/m^3
Portugal OEL - TWA	5 mg/m^3
Romania OEL - TWA	5 mg/m^3
Russia OEL - TWA	6 mg/m^3
Slovakia OEL - TWA	1.5 mg/m^3
Spain OEL - TWA	5 mg/m^3
Sweden OEL - TWAs	3.5 mg/m^3
Switzerland OEL -TWAs	3 mg/m^3
Vietnam OEL - TWAs	5 mg/m^3

Titanium dioxide

ACGIH Threshold Limit Value (TWA)	10 mg/m^3
Australia TWA	10 mg/m^3
Austria OEL - MAKs	5 mg/m^3
Belgium OEL - TWA	10 mg/m^3
Bulgaria OEL - TWA	10.0 mg/m^3
Denmark OEL - TWA	6 mg/m^3
Estonia OEL - TWA	5 mg/m^3
France OEL - TWA	10 mg/m^3
Greece OEL - TWA	10 mg/m^3
	5 mg/m^3
Ireland OEL - TWAs	10 mg/m^3
	4 mg/m^3
Latvia OEL - TWA	10 mg/m^3
Lithuania OEL - TWA	5 mg/m^3
OSHA - Final PELS - TWAs:	15 mg/m^3
Poland OEL - TWA	10.0 mg/m^3
Portugal OEL - TWA	10 mg/m^3
Romania OEL - TWA	10 mg/m^3
Russia OEL - TWA	10 mg/m^3
Spain OEL - TWA	10 mg/m^3
Sweden OEL - TWAs	5 mg/m^3
Switzerland OEL -TWAs	3 mg/m^3

8. EXPOSURE CONTROLS / PERSONAL PROTECTION

Vietnam OEL - TWAs	6 mg/m^3 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.
Hands:	Impervious gloves (e.g. Nitrile, etc.) are 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 goggles if eye contact is possible. (Eye protection must meet the standards in accordance with EN166, ANSI Z87.1 or international equivalent.) Wear safety goggles if eye contact is possible (face shield recommended if splashing is possible). (Eye protection must meet the standards in accordance with EN166, ANSI Z87.1 or international equivalent.)
Skin:	Impervious 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 half mask, P3 filter). (Respirators must meet the standards in accordance with EN140, EN143, ASTM F2704-10 or international equivalent.)

9. PHYSICAL AND CHEMICAL PROPERTIES

Physical State:	Capsule	**Color:**	White / Pink and Pink / Pink
Odor:	No data available.	**Odor Threshold:**	No data available.
Molecular Formula:	Mixture	**Molecular Weight:**	Mixture

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)
Crizotinib
Predicted 7.4 Log D 2.07
Dicalcium Phosphate
No data available
Microcrystalline cellulose
No data available
Silicium dioxide
No data available
Sodium starch glycolate
No data available
Magnesium stearate

9. PHYSICAL AND CHEMICAL PROPERTIES

No data available

Gelatin

No data available

Titanium dioxide

No data available

Ferric oxide red

No data available

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
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.
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: The information included in this section describes the potential hazards of the individual ingredients.

Known Clinical Effects: Based on clinical trials in humans, possible adverse effects following exposure to this compound may include: diarrhea, nausea, vomiting, fatigue, visual disturbances, and headache. Additionally, effects on liver, respiratory system, cardiovascular system may occur.

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

Microcrystalline cellulose

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

Magnesium stearate

Rat Oral LD50 > 2000 mg/kg
Rat Inhalation LC50 > 2000 mg/m^3

11. TOXICOLOGICAL INFORMATION

Titanium dioxide
Rat Oral LD50 > 7500 mg/kg
Rat Subcutaneous LD50 50 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)

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

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

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

Crizotinib
7 Day(s) Rat Oral 150 mg/kg/day NOAEL None identified
28 Day(s) Mouse Oral 200 mg/kg/day NOAEL None identified
1 Month(s) Rat Oral 10 mg/kg/day NOAEL Bone Marrow, Kidney, Male reproductive system
1 Month(s) Dog Oral 20 mg/kg/day NOAEL None identified
3 Month(s) Rat Oral (M) 100 / (F) 250 mg/kg/day LOAEL Male reproductive system, Bone Marrow, Liver, Gastrointestinal system, Pituitary
3 Month(s) Dog Oral 25 mg/kg/day NOAEL Blood

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

Crizotinib
Embryo / Fetal Development Rat Oral 200 mg/kg/day LOAEL Maternal toxicity, Developmental toxicity
Embryo / Fetal Development Rabbit Oral 60 mg/kg/day NOAEL Maternal Toxicity
Embryo / Fetal Development Rabbit Oral 60 mg/kg/day LOAEL Developmental toxicity

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

Crizotinib
Bacterial Mutagenicity (Ames) *Salmonella* , *E. coli* Negative
In Vitro Micronucleus Chinese Hamster Ovary (CHO) cells Positive without activation
In Vitro Chromosome Aberration Human Lymphocytes Positive
In Vivo Micronucleus Rat Bone Marrow Positive

Carcinogen Status: See below

Titanium dioxide
IARC: Group 2B (Possibly Carcinogenic to Humans)

Ferric oxide red
IARC: Group 3 (Not Classifiable)

11. TOXICOLOGICAL INFORMATION

12. ECOLOGICAL INFORMATION

Environmental Overview: Very toxic to aquatic organisms. Releases to the environment should be avoided.

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

Crizotinib
Cyprinodon variegatus (Sheepshead Minnow) OECD LC50 96 Hours > 5.2 mg/L
Skeletonema costatum (Marine Diatom) OECD EC50 72 Hours < 0.10-0.19 mg/L
Tisbe battagliai (Marine Copepod) OECD EC50 48 Hours 0.66 mg/L

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

Crizotinib
Activated sludge OECD EC50 > 1000 mg/L

Persistence and Degradability: No data available

Bio-accumulative Potential:
Partition Coefficient: (Method, pH, Endpoint, Value)
Crizotinib
Predicted 7.4 Log D 2.07

Mobility in Soil: No data available

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 (crizotinib)
Transport hazard class(es): 9
Packing group: III

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.

IMDG

Environmental Hazard(s): Marine Pollutant

15. REGULATORY INFORMATION

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

Crizotinib

CERCLA/SARA 313 Emission reporting	Not Listed
California Proposition 65	Not Listed
Standard for the Uniform Scheduling for Drugs and Poisons:	Schedule 4
EU EINECS/ELINCS List	Not Listed

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

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

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

15. REGULATORY INFORMATION

EU EINECS/ELINCS List	209-150-3

Gelatin

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	232-554-6

Silicium dioxide

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

Ferric oxide red

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	215-168-2

Titanium dioxide

CERCLA/SARA 313 Emission reporting	Not Listed
California Proposition 65	carcinogen 9/2/2011 airborne, unbound particles of respirable size
Inventory - United States TSCA - Sect. 8(b)	Present
Australia (AICS):	Present
EU EINECS/ELINCS List	236-675-5

16. OTHER INFORMATION

Text of CLP/GHS Classification abbreviations mentioned in Section 3

Serious eye damage/eye irritation-Cat.1; H318 - Causes serious eye damage
Sensitization, skin-Cat.1; H317 - May cause an allergic skin reaction
Germ cell mutagenicity-Cat.2; H341 - Suspected of causing genetic defects
Hazardous to the aquatic environment, acute toxicity-Cat.1; H400 - Very toxic to aquatic life

Data Sources:	Pfizer proprietary drug development information. Publicly available toxicity information.
Reasons for Revision:	Updated Section 14 - Transport Information.
Revision date:	08-Feb-2018
Prepared by:	Product Stewardship Hazard Communication Pfizer Global Environment, Health, and Safety Operations

Pfizer Inc believes that the information contained in this Material 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