MATERIAL SAFETY DATA SHEET

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

Pfizer Inc
Pfizer Pharmaceuticals Group
235 East 42nd Street
New York, New York 10017
1-212-573-2222

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

Material Name: Crizotinib Capsules

Trade Name: XALKORI
Chemical Family: Anaplastic Lymphoma Kinase Inhibitor
Intended Use: Pharmaceutical product for the treatment of lung cancer

2. HAZARDS IDENTIFICATION

Appearance: White and Pink Capsules
Signal Word: WARNING

Statement of Hazard:
May cause allergic skin reaction.
Suspected of causing genetic defects.
Causes severe eye irritation.
Very toxic to aquatic life.

Additional Hazard Information:
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.

EU Classification
EU Indication of danger:
Mutagenic: Category 3
Xi - Irritant
Dangerous for the Environment

EU Hazard Symbols:

EU Risk Phrases:
R41 - Risk of serious damage to eyes.
R43 - May cause sensitization by skin contact.
R68 - Possible risk of irreversible effects.
R50 - Very toxic to aquatic organisms.

2. HAZARDS IDENTIFICATION

Australian Hazard Classification (NOHSC): Hazardous Substance. Dangerous Goods.

Note: This document has been prepared in accordance with standards for workplace safety, which require the inclusion of all known hazards of the active substance or its intermediates regardless of the potential risk. The precautionary statements and warnings 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	EU Classification	%
Crizotinib	877399-52-5	Not Listed	Xi;R41 Xi;R43 Muta. Cat.3;R68 N,R50	50
Microcrystalline cellulose	9004-34-6	232-674-9	Not Listed	*
Dicalcium Phosphate	7757-93-9	231-826-1	Not Listed	*
Magnesium stearate	557-04-0	209-150-3	Not Listed	*

Ingredient	CAS Number	EU EINECS/ELINCS List	EU Classification	%
Silicium dioxide	Not Assigned	Not Listed	Not Listed	*
Sodium starch glycolate	9063-38-1	Not Listed	Not Listed	*
Hard gelatin capsules	MIXTURE	Not Listed	Not Listed	*

Additional Information: * Proprietary
Ingredient(s) indicated as hazardous have been assessed under standards for workplace safety.

For the full text of the R phrases mentioned in this Section, see Section 16

4. 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.

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.

5. FIRE FIGHTING MEASURES

Extinguishing Media: Use carbon dioxide, dry chemical, or water spray.

Hazardous Combustion Products: Formation of toxic gases is possible during heating or fire.

Fire Fighting Procedures: During all fire fighting activities, wear appropriate protective equipment, including self-contained breathing apparatus.

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

6. ACCIDENTAL RELEASE MEASURES

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

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.

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

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

7. HANDLING AND STORAGE

General 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.

Storage Conditions: Store as directed by product packaging.

8. EXPOSURE CONTROLS / PERSONAL PROTECTION

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

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
Spain OEL - TWA	10 mg/m^3

8. EXPOSURE CONTROLS / PERSONAL PROTECTION

Dicalcium Phosphate

Latvia OEL - TWA	10 mg/m^3

Magnesium stearate

ACGIH Threshold Limit Value (TWA)	10 mg/m^3
Lithuania OEL - TWA	5 mg/m^3
Sweden OEL - TWAs	5 mg/m^3

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.

Environmental Exposure Controls: Refer to specific Member State legislation for requirements under Community environmental legislation.

Personal Protective Equipment: Refer to applicable national standards and regulations in the selection and use of personal protective equipment (PPE).

Hands: Impervious gloves are recommended if skin contact with drug product is possible and for bulk processing operations.

Eyes: Wear safety goggles if eye contact is possible.

Skin: Impervious protective clothing is recommended if skin contact with drug product is possible and for bulk processing operations.

Respiratory protection: 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.

9. PHYSICAL AND CHEMICAL PROPERTIES

Physical State:	Capsule	**Color:**	White / Pink and Pink / Pink
Molecular Formula:	Mixture	**Molecular Weight:**	Mixture

Partition Coefficient (Measured - Log Pow/Log Kow): 1.83

10. STABILITY AND REACTIVITY

Chemical Stability: Stable under normal conditions of use.

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

11. TOXICOLOGICAL INFORMATION

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

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

Magnesium stearate
Rat Oral LD50 > 2000 mg/kg

11. TOXICOLOGICAL INFORMATION

Rat Inhalation LC50 > 2000 mg/m^3

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

Dicalcium Phosphate
Rat Oral LD 50 10 g/kg
Rabbit Dermal LD 50 >7940 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

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

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

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

12. ECOLOGICAL INFORMATION

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

Partition Coefficient (Measured - Log Pow/Log Kow): 1.83

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

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

15. REGULATORY INFORMATION

EU Symbol: Xn , Xi N
EU Indication of danger: Mutagenic: Category 3
Xi - Irritant
Dangerous for the Environment

EU Risk Phrases:

R41 - Risk of serious damage to eyes.
R43 - May cause sensitization by skin contact.
R68 - Possible risk of irreversible effects.
R50 - Very toxic to aquatic organisms.

EU Safety Phrases:

15. REGULATORY INFORMATION

S22 - Do not breathe dust.
S24/25 - Avoid contact with skin and eyes.
S36/37/39 - Wear suitable protective clothing, gloves and eye/face protection.

OSHA Label:
WARNING
May cause allergic skin reaction.
Suspected of causing genetic defects.
Causes severe eye irritation.
Very toxic to aquatic life.

Canada - WHMIS: Classifications

WHMIS hazard class:
D2b toxic materials

Sodium starch glycolate

Inventory - United States TSCA - Sect. 8(b)	Present
Australia (AICS):	Present

Microcrystalline cellulose

Inventory - United States TSCA - Sect. 8(b)	Present
Australia (AICS):	Present
EU EINECS/ELINCS List	232-674-9

Dicalcium Phosphate

Inventory - United States TSCA - Sect. 8(b)	Present
Australia (AICS):	Present
EU EINECS/ELINCS List	231-826-1

Magnesium stearate

Inventory - United States TSCA - Sect. 8(b)	Present
Australia (AICS):	Present
EU EINECS/ELINCS List	209-150-3

16. OTHER INFORMATION

Text of R phrases mentioned in Section 3

R41 - Risk of serious damage to eyes.
R43 - May cause sensitization by skin contact.
R68 - Possible risks of irreversible effects.
R50 - Very toxic to aquatic organisms.
Data Sources: Pfizer proprietary drug development information. Publicly available toxicity information.

Reasons for Revision: Updated Section 8 - Exposure Controls / Personal Protection. Updated Section 2 - Hazard Identification. Updated Section 15 - Regulatory Information.

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